ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE ENGINEERING AND TECHNOLOGY

MODIFICATION OF PENDANT ANTHRACENE AND AZIDE FUNCTIONALIZED POLYCARBONATES VIA DOUBLE CLICK REACTIONS

M.Sc. THESIS

Sümeyra YOLDAŞ

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İSTANBUL TEKNİK ÜNİVERSİTESİ ★ FEN BİLİMLERİ ENSTİTÜSÜ

ANTRASEN VE AZİD YAN GRUPLARI İÇEREN POLİKARBONATLARIN İKİLİ 'CLİCK' REAKSİYONLARI İLE MODİFİKASYONU

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MAYIS 2014

Sümeyra YOLDAŞ, a **M.Sc.** student of ITU **Graduate School of Science Engineering and Technology** student ID **509121078**, successfully defended the **thesis** entitled "**Modification of Pendant Anthracene and Azide Functionalized Polycarbonates Via Double Click Reactions**", which he prepared after fulfilling the requirements specified in the associated legislations, before the jury whose signatures are below.

Thesis Advisor : **Prof. Dr. Gürkan HIZAL**
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Date of Submission : 05 May 2014
Date of Defense : 28 May 2014

To my family,

FOREWORD

This master study has been carried out at Istanbul Technical University, Chemistry Department of Science & Letter Faculty.
I would like to express my gratitude to my thesis supervisor, Prof. Dr. Gürkan HIZAL and co-supervisor Prof. Dr. Ümit TUNCA for offering invaluable help in all possible ways, continuos encouragement and helpful critisms throughout this research.
I would like to express my special thanks to Assoc. Prof. Dr. Hakan DURMAZ, Assoc. Prof. Dr. Aydan DAĞ, Res. Assist. Ufuk Saim GÜNAY, M.Sc. Pınar Sinem OMURTAG, M.Sc. Bilal Buğra UYSAL and Res. Assist. Neşe ÇAKIR for their helpful and understanding attitudes during my laboratory and thesis study in ITU. It has been a pleasure to work with them.
I would like to thank my colleagues Gizem PALAK, Gökçe MİHLAÇ, Burcu YILMAZ, Erhan DEMİREL, Hande TINAS, Meir ABUAF, Lale ATICI, and for their friendly and helpful attitude during my laboratory works.
I would like to thank my all labmates for their help. It was really a great pleasure for me to know all of you. I am sure that we will always be in touch rest of our lives as well.
I would like to offer the most gratitude to my family for their patience, understanding and morale support during all stages involved in the preparation of this research.They are wonderful beings in moving me to realize and achieve the things I have dreamed.

May 2014

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ABBREVIATIONS

^{1}H NMR	**:**Hydrogen Nuclear Magnetic Resonance Spectroscopy
ATRP	**:**Atom Transfer Radical Polymerization
CH_2Cl_2	**:**Dichloro methane
$CHCl_3$	**:**Chloroform
$CDCl_3$	**:**Deuterated chloroform
CuAAC	**:**Copper(I) catalyzed azide-alkyne cycloaddition
DA	**:**Diels-Alder
DBU	**:**1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	**:**Dichloromethane
DMAP	**:**4-dimethylaminopyridine
FPT	**:**Freeze-Pump-Thaw
GPC	**:**Gel Permeation Chromatography
PEG	**:**Poly(ethyleneglycol)
PC	**:**Poly(carbonate)
PCL	**:**Poly(ε-caprolactone)
ROP	**:**Ring-opening polymerization
p-TSA	**:**p-Toluene sulfonic acid
THF	**:**Tetrahydrofuran
TU	**:**Thiourea
TU/A	**:**Thioureaamine
UV	**:**Ultra Violet

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MODIFICATION OF PENDANT ANTHRACENE AND AZIDE FUNCTIONALIZED POLYCARBONATES VIA DOUBLE CLICK REACTIONS

SUMMARY

Biocompatible, biodegradable, or bioresorbable polymers uses in biomedical and environmental applications, such as medical implants and drug-delivery systems. As a kind of surface erosion biodegradable materials, aliphatic polycarbonates are usually derived from ring-opening polymerization (ROP) and have gained increasing interest for their potential use in biomedical and pharmaceutical applications due to their favorable biocompatibility, biodegradability, and nontoxicity.

The ionic polymerizations (anionic or cationic) were the only living systems available until last decade. Contolling molecular weight, well-defined chain ends, and low polydispersity are the most usefull advantages of controlling/living polymerization systems. Atom transfer radical polymerization (ATRP), nitroxide mediated radical polymerization (NMP), and reversible addition-fragmentation chain transfer polymerization (RAFT) are most widely used methods for C/LRP.

Nowadays, alternative routes such as Diels-Alder (DA) and the copper catalyzed azide-alkyne cycloaddition (CuAAC) click reactions which can be classified under the term "click chemistry" have emerged as a powerful tool for the preperation of block and graft copolymers.

One of the most used strategie is copolymerization which has developed as to adjust the properties of polymeric materials. The combination of two polymers into a single entity is generally advantageous because the copolymers may integrate the merits of the original homopolymers. Graft copolymers, also called molecular brushes, have attracted considerable interest for their distinguished conformation and properties.

In this study, anthracene and azide functional cyclic carbonate monomers are synthesized, the *co*-polymerization of these was carried out successfully via ring-opening polymerization (ROP) using benzyl alcohol as initiator, 1,8-diazabicyclo[5.4.0]undec-7-ene and 1-(3,5-bis(trifluorometh1-(3,5-bis(trifluoromethyl))-3-cyclohexyl-2-thiourea, as catalyst system.

Subsequently, anthracene and azide functional polycarbonate chain, copper catalyzed azide-alkyne cycloaddition (CuAAC) by reaction of Alkyne-PCL, and Diels-Alder (DA) by reaction maleimide end-functionalized PEG attaching and PC-*g*-PCL/PEG heterograft copolymer was obtained.

Diels-Alder click reaction efficiency for graft copolymerization was monitored by UV-Vis spectroscopy. The structures of all monomers, initiators, polymer precursors and final polymers were confirmed exactly using GPC, ^{1}H NMR, UV-Vis and FT-IR analyses.

ANTRASEN VE AZİD YAN GRUPLARI İÇEREN POLİKARBONATLARIN İKİLİ 'CLİCK' REAKSİYONLARI İLE MODİFİKASYONU

ÖZET

Biyolojik olarak uyumluluk, kolay parçalanabilme veya yüksek emilim gibi birtakım özellikli polimerlere olan ilgi son zamanlarda artmıştır. Bu polimerler medikal implantlar ve ilaç-taşıma sistemleri gibi biyomedikal ve çevresel uygulama alanlarında kullanılmaktadır. Yüzey erozyonunun bir çeşidi olan biyo çözünür malzemelerin bir çeşidi olan alifatik polikarbonatlar genellikle halka açılma polimerizasyonu (ROP) yoluyla elde edilir. Ayrıca sahip oldukları biyolojik uyumluluk, kolay parçalanabilme ve toksik olmama özelliklerinden dolayı biyomedikal ve ilaç uygulamalarında tercih edilir.

Aşı polimerler sahip olduğu lineer olmayan yapısı, farklı bileşimi ve topolojisi nedeniyle önemli bir ilgiye sahiptir. Dallı yapılarından dolayı genellikle düşük vizkozite değerlerine sahiptir ve bu durumda polimerin işlenme koşullarını kolaylaştırır. Ayrıca, aşı polimerler lineer polimerlere kıyasla daha iyi fiziksel ve kimyasal özelliklere sahiptirler. Son yıllara kadar, elde bulunan sistemler yaşayan iyonik polimerizasyonlardı (anyonik ve katyonik) . Bu sistemler sayesinde moleküler ağırlığı kontrol edilebilen, well- defined zincir sonu olan ve düşük polidipersiteye sahip polimerler elde edilebilir. Son yıllarda ise kompleks makromoleküllerin sentezinde kullanılan kontrollü/yaşayan polimerizasyon metotlarının kullanımı arttı. İyonik polimerizasyona göre monomerlerin fazla çeşitli olması ve deney koşullarının daha rahat olması bunun başlıca sebebidir.

Son yıllara kadar, elde bulunan sistemler yaşayan iyonik polimerizasyonlardı (anyonik ve katyonik). Bu sistemler sayesinde moleküler ağırlığı kontrol edilebilen, zincir sonu olan ve düşük polidipersiteye sahip polimerler elde edilebilir. Son yıllarda ise kompleks makromoleküllerin sentezinde kullanılan kontrollü/yaşayan polimerizasyon metotlarının kullanımı arttı. İyonik polimerizasyona göre monomerlerin fazla çeşitli olması ve deney koşullarının daha rahat olması bunun başlıca sebebidir.

Bir nevi katılma polimerizasyon mekanizmasına sahip olan yaşayan polimerizasyon reaksiyonlarında büyüyen polimer zincirinin sonlanma adımı ortadan kaldırılmıştır. Daha doğrusu, sonlanma ve başlama basamakları dış etmenlerle kontrollü bir şekilde yapılır. Bu sayede polimerin molekül ağırlığı ve polimer zincirlerinin zincir sonu grupları kontrol edilir. Zincir sonuna eklenebilecek farklı fonksiyonellikte gruplar ile polimerin fiziksel özellikleri uyumlaşabilir.

Sonlanma ve zincir transferi reaksiyonlarının olmadığı yaşayan polimerizasyon mekanizmalarında polimer zincirinin büyüme hızı (hemen hemen) sabittir ve reaksiyon sonunda elde edilen polimer moleküllerinin zincir büyüklükleri birbirine çok yakındır; yani monodisperse yakın molekül ağırlığı dağılımı vardır.

Genel olarak serbest radikal polimerizasyonunda polimer zincirleri ilk adımlarda hızla büyüdükleri halde , kontrollü radikal polimerizasyonda polimer zincirlerinin büyümesi doğrusal bir yol izler.

Kontrollü /yaşayan polimerizasyon tekniklerinden biri olan ATRP kendinden önceki önceki kontrollü radikal polimerizasyon yöntemlerinden (iyonik ,kararlı serbest radikal polimerizasyonu gibi), karmaşık polimer yapıları üretimine izin vermesi ile ayrılır.Bu polimerizasyon yöntemi, sıcaklık gibi reaksiyon parametrelerinin kontrolü ile kolayca durdurulup yeniden başlatılabilir. ATRP'den önce ortaya çıkan kontrollü polimerleşme yöntemlerinde her çeşit monomer kullanılamamasına karşın, ATRP mekanizmasında geniş bir monomer yelpazesine kullanılabilir. Kontrollü ve düzenli büyüyen polimer zinciri ve düşük molekül ağırlığı dağılımı (*polidispersite*), ATRP mekanizması sırasında kullanılan metal bazlı katalizör sayesinde elde edilir.

Halka açılma polimerizasyonu (ROP) siklik monomerin lineer polimer oluşturmak üzere açıldığı tek polimerizasyon yöntemidir. Lactide, carbonate gibi siklik esterlerin halka açılma polimerizasyonu kontrollü poliester sentezinde genel ve etkin bir metottur. Polimerizasyon yöntemlerine ek olarak, düşük polidispersite indisleri ve uç gruplarda yüksek uyumluluk gibi birçok gelişmiş uygulama, ağır metaller gibi istenmeyen kirliliklerin katalizörlerden uzaklaştırılmasını gerektirir. Bu amaçla siklik esterlerin metalsiz halka açılma reaksiyonlarına organokatalitik yaklaşımlarda bulunulmuştur. Günümüzde, "click kimyası" terimi altında sınıflandırılan Diels-Alder (DA) ve bakır katalizli azid-alkin siklokatılma (CuAAC) tepkimeleri blok ve aşı kopolimerlerden karmaşık makromoleküler yapılara kadar değişen birçok polimerik malzemenin sentezinde başarılı bir şekilde uygulandı ve blok, aşı ve yıldız polimerlerin eldelerinde güçlü bir alternatif yöntem olarak ortaya çıktı.

Click kimyası hızlı, etkin, güvenilir ve seçici olmak gibi özelliklere sahip olmasının yanı sıra yeni ilaç araştırma ve biyokimya çalışmalarında geniş olarak kullanılır. Click kimyasında en popüler reaksiyonlardan biri Huisgen 1,3-dipolar siklik katılması reaksiyonudur. Oda sıcaklığında olan azid ve alkin nin reaksiyonunda Cu(I) kataliz olarak kullanılır. Bu reaksiyonun çok tercih edilmesinin sebebi reaksiyon şartlarının basit olması, yan ürün olmaması, verimin yüksek olması ve saflaştırmanın kolay olmasıdır. Bu reaksiyon mekanizması ile ilgili Emrick in yaptığı ilk çalışmalardan bu yana, biyolojik olarak ile ilgili olarak click kimyası ve halka açılma polimerizasyonu metotlarının kullanıldığı bir çok çalışma yapılmıştır. Fakat, click kimyası kullanılarak polikarbonatların modifikasyonun içeren çalışmaların sayısı azdır.

Kopolimerizasyon, polimerik malzemelerin özelliklerini değiştirme ve ayarlamada kullanılan önemli bir yöntemdir. İki polimerin tek olacak şekilde bir araya gelmesi, kopolimerlerin orijinal polimerin meritlerine kadar girebilmesi nedeniyle avantajlıdır. Aşı kopolimerler, moleküler fırça olarak da bilinirler, sahip oldukları özellikler ve şekilleri sayesinde oldukça popülerdirler.

Basit halka açılma kopolimerizasyonu ile kontrollü olarak fiziksel ve mekanik özellikleri belirlenebilen polikarbonat kopolimerler elde edilir. Karbonatların halka açılma polimerizasyonu ile yüksek kaliteli (yüksek moleküler ağırlık ve düşük polidispersite) polikarbonatların elde edilmesi oldukça oldukça efektif bir metottur. Bu çalışmada, belirlenebilir moleküler ağırlığa ve yapıya sahip olan PC-Anth aşı kopolimerlerinin dizaynı ve sentezi konu edilmiştir ve antrasen-maleimid-bazlı DA "click reaksiyonu" aşı kopolimer hazırlanmasında kullanılmıştır.

Siklik karbonat monomerlere pentaflorofenilester, azid, allil, alkil halojenür, hidroksil (met)akrilat, stiren, furan, maleimid, ve vinil gibi fonksiyonel grupların eklenmesi, sonuçta elde edilen polikarbonatların fiziksel, kimyasal ve biyolojik özellikleri üzerinde etkin bir denetim sağlar. Ayrıca polikarbonatlardaki bu asılı fonksiyonel grupların yüksek etkinlikli "click" tepkimeleri ile tekrar türevlendirilmeleri iyi tanımlanmış son ürünlerin eldesine yol açacaktır.

Antrasen ve azid fonksiyonlu halkalı karbonat monomerleri sentezlenerek, *ko*-polimerizasyonu, benzil alkol başlatıcılığında, 1,8-diazabisiklo[5.4.0]undek-7-en ve 1-(3,5-bis(trifloromethil)fenil)-3-siklohekzil tiyoüre katalizörlüğündeki halka açılma polimerizasyonu ile gerçekleştirilmiştir.

Çalışmanın sonraki kısmında antrasen ve azid fonksiyonlu polikarbonat zincirine bakır katalizli azid-alkin siklokatılma (CuAAC) reaksiyonu ile Alkin-PCL ve Diels-Alder (DA) reaksiyonu ile maleimid uç fonksiyonlu PEG takılarak PC-*g*-PCL/PEG aşı kopolimeri elde edildi. Aşı kopolimerleri için Diels-Alder reaksiyon etkinliği UV-Vis spektroskopisi yardımıyla belirlendi. Elde edilen monomerler, öncü bileşikler, başlangıç polimerleri ve sonuç polimerler ^{1}H NMR, UV, FT-IR ve GPC kullanılarak analiz edilmiştir.

1. INTRODUCTION

Polymer properties are mainly influenced by the chemical composition, functionality, molecular weight and topology of the constituting macromolecules [1]. Therefore, the synthesis of well-defined complex macromolecular structures, such as stars, dendrimers, graft and cyclic polymers, to control the polymer properties is a key field of study in polymer science [1].

Graft copolymers with a large number of side chains chemically attached onto a linear backbone are endowed with unusual properties thanks to their confined and compact structures, including wormlike conformation, compact molecular dimensions and notable chain end effects [2].

Graft copolymers can be obtained with three general methods: (i) grafting-onto, in which side chains are preformed, and then attached to the backbone; (ii) grafting-from, in which the monomer is grafted from the backbone; and (iii) grafting-through, in which the macromonomers are copolymerized [3-4].

Ring-opening polymerization (ROP) is a unique polymerization process, in which a cyclic monomer is opened to generate a linear polymer. Polymers with a wide variety of functional groups can be produced by ring-opening polymerizations. Preparation of cyclic monomers, studies of catalysis and mechanisms are active areas of research both in academia and industry[5-8].

Click chemistry has been used extensively due to its quantitative yields, high tolerance of functional groups, and insensitivity of the reaction to solvents [9]. The reaction between a terminal alkyne and an azide groups to form a triazole group is the most popular one, which was first studied by Huisgen [10]. Nowadays, click reactions have already been widely used in polymeric science and material, such as the synthesis of linear, dendritic, cyclic, and star polymers [11-12].

It is quite favorable since cyclic carbonates have a variety of advantages in the light of actual applications, such as ease of molecular design and synthesis, diversity of polymerization mode, mild polymerization condition, high polymerization

efficiency, and so on, in comparison with the hitherto recognized expandable monomers [13-14]. So, it can be expected that cyclic carbonates may be utilized in many polymer material fields.

This strategy is particularly attractive for ring-opening polymerization (ROP) as the inventiory of carbonate monomers available are limited. To improve hydrophilicity, degradation rate, and mechanical properties of polycarbonates, various functional groups such as carboxyl [15-17], amino [18-20], hydroxyl [21-22], etc. were introduced through copolymerization with functional carbonate monomers.

Thiol-ene, and copper catalyzed azide-alkyne cycloaddition (CuAAC) reactions have been utilized only for the postpolymerization functionalization of the PCs[22-25]. Recently, we applied Diels-Alder reaction to the preparation of well-defined PC-graft copolymers[26].

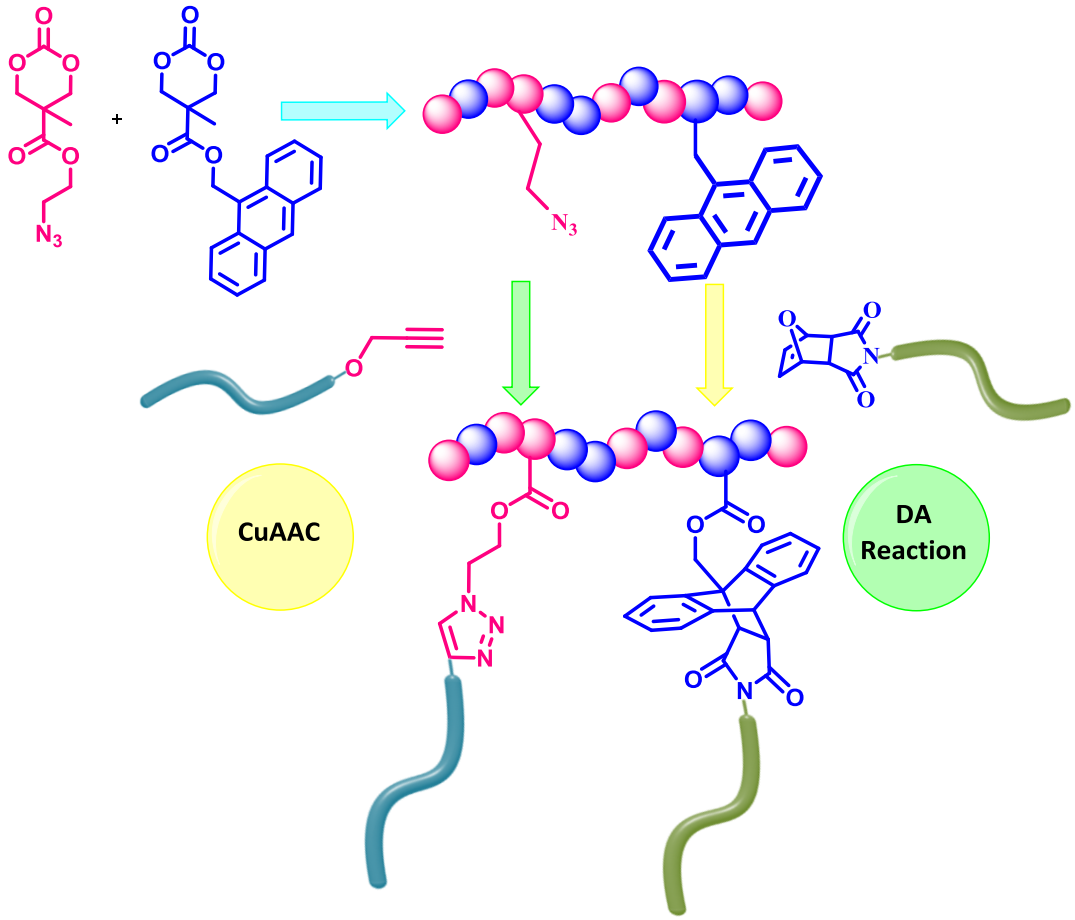


Figure 1.1 : Synthesis of graft copolymers via ROP, Diels-Alder click reaction and CuAAC click reaction.

In this thesis, the copolymerization of anthracene- and azide-functional cyclic carbonate monomers were carried out successfully via ring-opening polymerization (ROP) using benzyl alcohol as initiator, 1,8-diazabicyclo[5.4.0]undec-7-ene and 1-(3,5-bis(trifluorometh1-(3,5-bis(trifluoromethyl))-3-cyclohexyl-2-thiourea, as catalyst system. In the following study, modification reactions of the anthracene- and azide- functional polycarbonate were accomplished under facile conditions via click reactions (CuAAC and Diels-Alder). Diels-Alder click reaction efficiency for graft copolymerization was monitored by UV-Vis spectroscopy.

2. THEORETICAL PART

2.1 Living Polymerization

The name "living polymerization" was coined for the method by Szwarc in 1956 [27] because the chain ends remain active untilled killed. (The term has nothing to do with living in the biological sense.) Before Szwarc's classical work, Flory [28] had described the properties associated with living polymerization of ethylene oxide initiated with alkoxides. Flory noted that since all of the chain ends grow at the same rate, the molecular weight is determined by the amount of initiator used versus monomer (Eq.1).

Degree of polymerization = [monomer]/[initiator] **(1)**

Another property of polymers produced by living polymerization is the very narrow molecular weight distribution [28]. The polydispersity (PDI) has a Poisson distribution, PDI = M_w/M_n; M_w and M_n can be determined by gel permeation chromatography (GPC).

A living polymerization can be distinguished from free radical polymerization or from a condensation polymerization by plotting the molecular weight of the polymer versus conversion. In a living polymerization, the molecular weight is directly proportional to conversion (Figure, 2.1 (A)). In a free radical or other nonliving polymerization, high molecular weight polymer is formed in the initial stages (Figure, 2.1(B)), and in a condensation polymerization, high molecular weight polymer is formed only as the conversion approaches 100% (Figure 2.1, (C)) [29].

Living polymerization provides end-group control and enables the synthesis of block copolymers by sequential monomer addition. However, it does not necessarily provide polymers with molecular weight (MW) control and narrow molecular weight distribution (MWD). To obtain well defined polymers the initiator should be consumed at early stages of polymerization and that the exchange between species of various reactivities should be at least as fast as propagation [30-32].

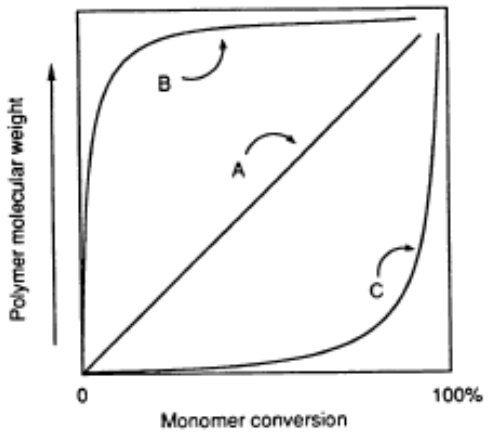


Figure 2.1 : Molecular weight conversion curves for various kinds of polymerization methods: (A) living polymerization; (B) free radical polymerization; and (C) condensation polymerization.

Much of the academic and industrial research on living polymerization has focused on anionic, cationic, coordination, and ring-opening polymerizations. The development of controlled/living radical polymerization (CRP) methods has been a long-standing goal in polymer chemistry, as a radical process is more tolerant of functional groups and impurities and is the leading industrial method to produce polymers [33]. Despite its tremendous industrial utility, CRP has not been realized until recently, largely due to the inevitable, near diffusion-controlled bimolecular radical coupling and disproportionation reactions.

2.2 Controlled/Living Polymerization

Macromolecular engineering of polymers with well-defined and applications through composition, size (molecular weight), uniformity (polydispersity), topology and end-functionality is essential to modern synthetic polymer chemistry research and advanced technological applications [34-40].

Nearly vast part of commercial synthetic polymers is made by using conventional free radical polymerization (FRP), which has so many advantages such as the polymerization of numerous vinyl monomers under mild reaction conditions, requiring an oxygen free medium, also tolerant to water, and a large temperature range (-80 to 250 ^{o}C) [33]. But it has some limitations, particularly in comparison with living processes [41,42].

The term of living polymerization is a chain growth polymerization. An ideal' living system is that the growing chain end propagates without chain transfer and termination. Szwarc et al. reported the first living polymerization in 1956, which was the anionic polymerization of styrene with sodium naphthalenide [43,44]. Well-defined polymers with uniform size, desired functionalities and various architectures have been increasingly achieved via living ionic polymerization. However, ionic polymerizations typically require stringent reaction conditions and have a limited range of (co)polymerizable monomers [45]. Following developments in living anionic polymerization by Michael Szwarc, new approaches towards synthesis of macromolecular engineered materials termed as controlled/"living" radical polymerizations (C/LRP) have been developed [46-48]. Mechanistically, C/LRPs are similar to FRP and proceed through the same intermediates. However, in C/LRPs the equilibrium between active and dormant species allows steadily growth of polymer chains via near instantaneous initiation and chain breaking reactions is minimized [47,49]. There are three classes of C/LRP, i.e. nitroxide mediated polymerization (NMP) [50,51] atom transfer radical polymerization (ATRP) [52-56], and reversible addition-fragmentation chain transfer (RAFT) polymerization [56,57].These methods have been known as powerful tools for preparing polymers with predetermined molecusdlar weights, narrow molecular weight distributions, specific end functionalities, and well- defined architectures [51].

2.3 Ring-Opening Polymerization (ROP)

Ring-opening polymerization (ROP) is a unique polymerization process, in which a cyclic monomer is opened to generate a linear polymer. It is fundamentally different from a condensation polymerization in that there is no small molecule byproduct during the polymerization. Polymers with a wide variety of functional groups can be produced by ring-opening polymerizations. Preparation of cyclic monomers, studies of catalysis and mechanisms are active areas of research both in industry and academia[5,8,23,24].

Nowadays, increasing attention is paid to degradable and biodegradable biocompatible polymers for applications in the biomedical and pharmaceutical fields, primarily because after use they can be eliminated from the body via natural pathways and also they can be a solution to problems concerning the global

environment and the solid waste management. Aliphatic polyesters are among the most promising materials as biodegradable polymers.

There are some reasons for studying the polymerization of cyclic esters. Firstly, to take advantage of the potential of preparing variety of polymers with control of the major variables affecting polymer properties in synthetic polymer. In addition, there are some important factors such as economy, toxicology, and technical apparatus development. Secondly, ROP facilitates to synthesise various advanced macromolecules, involving homopolymers with well-defined structures or end groups, or copolymers such as block, graft or star copolymers[58].

2.3.1 Controlled Ring-Opening Polymerization of cyclic esters

Aliphatic poly(ester)s are prepared through one of two routes: the first is step-growth polycondensation of a hydroxy acid or between a diacid and a diol. The second route is ring-opening polymerization (ROP). It is a unique polymerization process, in which a cyclic monomer is opened to generate a linear polymer, e.g., ROP of ε-caprolactone (CL) (Figure 2.2). ROP is a chain polymerization, comprise of a sequence of initiation, propagation and termination, so different from step polymerization. Altough ROP like as living polymerization because of increasing molecular weigth linearly with conversion [59], it differs from chain polymerizations due to reaction kinetics. By this methodology the preparation of high molecular weight aliphatic poly(ester)s is possible while maintaining high levels of control over their molecular characteristics under relatively mild conditions.

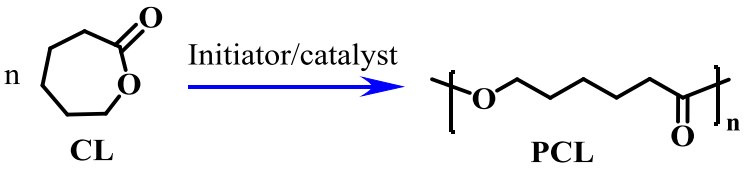


Figure 2.2 : ROP of ε-caprolactone (CL) [59].

Catalysts

A large variety of organometallic compounds, such as metal alkoxides and metal carboxylates, has been studied as initiators or catalysts in order to achieve effective polymer synthesis[60]. The covalent metal alkoxides with free p or d orbitals react as coordination initiators and not as anionic or cationic initiators[61]. The most widely used complex for the industrial preparation of polylactones and polylactides is

undoubtedly tin(II)2-ethylhexanoate, commonly referred as stannous octoate [$Sn(Oct)_2$]. It has been approved as a food additive by the American Food and Drug Administration (FDA)[58]. It is also commercially available, easy to handle and soluble in common organic solvents and in melt monomers. It is highly active and allows for the preparation of high-molecular-weight polymers in the presence of an alcohol[62]. Aluminum alkoxides have also proved to be efficient catalysts for the ROP of cyclic esters. The common example, namely, aluminum (III) isopropoxide, $Al(Oi\text{-}Pr)_3$, has been largely used for mechanistic studies. However, it has been revealed to be significantly less active than $Sn(Oct)_2$[63]. Moreover, an induction period of a few minutes is systematically observed with $Al(Oi\text{-}Pr)_3$ attributed to aggregation phenomenon[64].

For all these reasons, $Al(Oi\text{-}Pr)_3$ is much less used for the preparation of biodegradable polyesters, and especially since aluminum ions do not belong to the human metabolism and are suspected of supporting Alzheimer's disease.

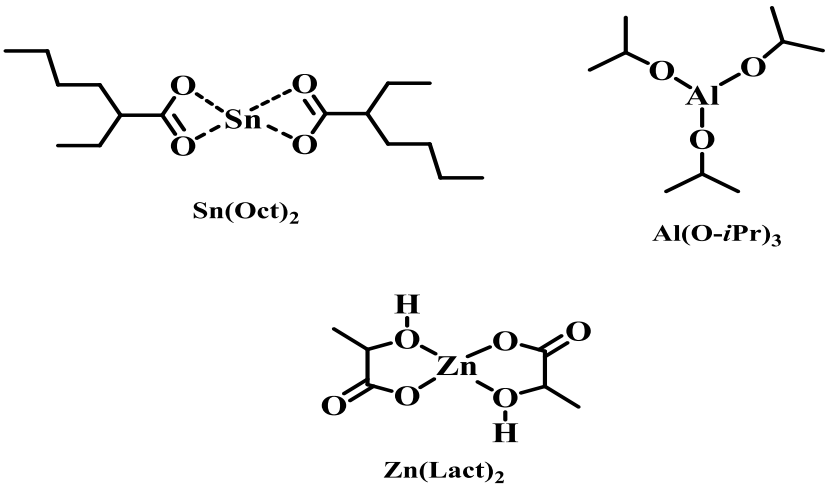
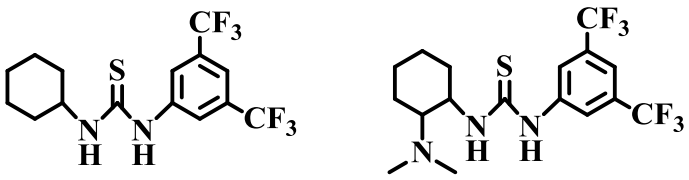


Figure 2.3 : Catalysts for ROP.

Much interest has been devoted to zinc derivatives as potential nontoxic catalysts. Zinc powder itself is a relatively good polymerization catalyst that is used industrially[65]. With reaction times of several days at 140 °C in bulk, it is roughly as active as $Al(Oi\text{-}Pr)_3$. Numerous zinc salts have also been investigated[66].

Although polymerization of alifatic cyclic carbonetes has been reported using organometallic catalysts (MAO, IBAO, $Sn(Oct)_2$ and $Al(Oi\text{-}Pr)_3$) and as well as enzymes, there are some metal-free catalysts polymerizations of carbonetes and other cyclic monomers such as lactones.



bis(3,5-triflouromethyl) phenylcyclohexyl thiourea cocatalyst (TU)

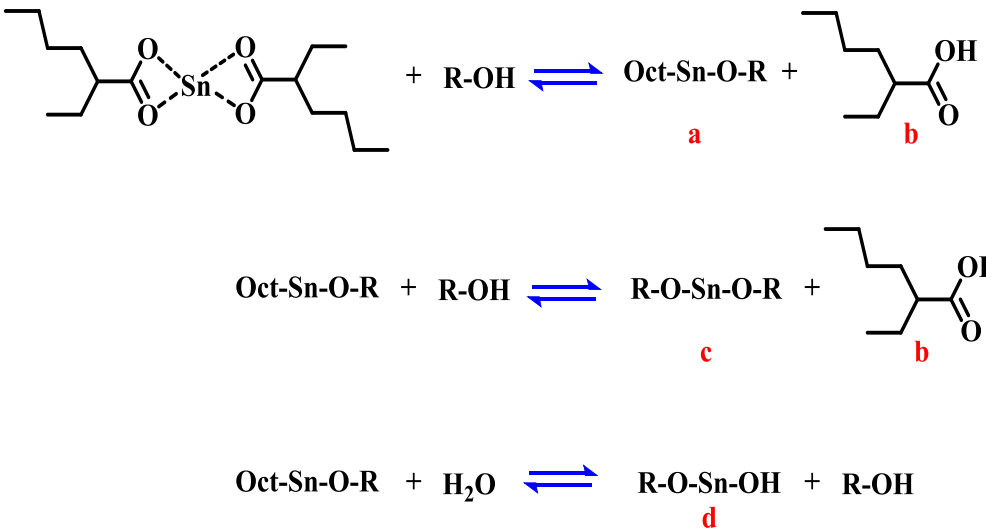
Thiourea-amine

Figure 2.4 : Amine Substituted Ureas and Thioureas Catalysts for ROP.

Both using bis(3,5-triflouromethyl) phenylcyclohexyl thiourea cocatalyst (TU) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) caused to quantitative monomer conversion in much shorter times while maintainng the excellent control over the polyester molecular parameters [67].

2.3.2 Coordination-Insertion Ring Opening Polymerization

Covalent metal carboxylates, particularly tin(II) bis(2-ethylhexanoate) usually referred to as tin(II) octanoate, $Sn(Oct)_2$ belong to the most frequently used initiators for polymerization of cyclic esters due to its low cost, low toxicity, and high efficiency. Although, there are controversial reports in the literature about the nature of $Sn(Oct)_2$ activity in the polymerization of lactones, two basic types of mechanism have been proposed. The first one is directly catalytic type where the catalyst serves to activate monomer through coordination with its carbonyl oxygen [68,69]. The second mechanism is the monomer insertion type mechanism where the catalyst acts as co-initiator along with either purposely added or adventitious hydroxyl impurities, and polymerization proceeds though an activated stannous alkoxide bond [70,71].



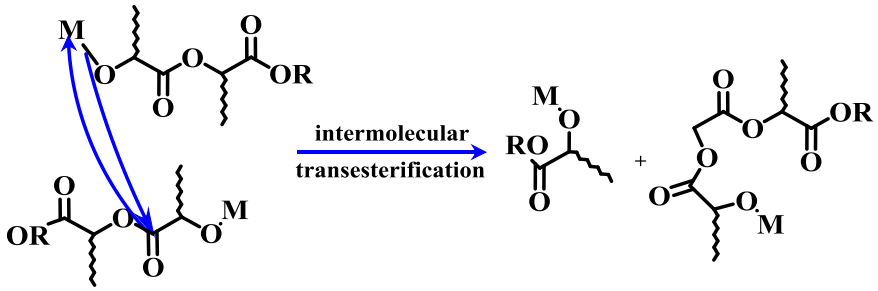
Kricheldorf and co-workers have recently illustrated how the structure of the alcohol initiator may influence the strength of the catalyst/alcohol interaction [69,71]. According to these authors, this interaction, in the early stages of reaction, is responsible for formation of the "true" initiating species, subsequent ring opening, and formation of the active, propagating chain end. Prior to the beginning of polymerization, adventitious hydroxyfunctional impurities (e.g., water) or purposely added alcohol first complex and subsequently react with $Sn(Oct)_2$ producing a stannous alkoxide species (a) and free 2-ethylhexanoic acid (b) as shown in 2.1. Further reaction with a second equivalent of alcohol produces the stannous dialkoxide initiator (c) and releases a second equivalent of 2-ethylhexanoic acid (b) as depicted in 2.1[71,72]. Adventitious water, meanwhile, serves mainly as a catalyst deactivator via a reversible reaction with a or c, thereby decreasing the concentration of active initiator and producing a stannous alcohol derivative (d), such as shown in 2.1, which is more thermodynamically stable than the stannous dialkoxide and is less efficient as an initiator [71].

In such coordination-insertion polymerizations, the efficiency of the molecular-weight control depends from the ratio $k_{propagation}/k_{initiation}$ but also from the extent of transesterification side reactions. These transesterification reactions can occur both intramolecularly (backbiting leading to macrocyclic structures and shorter chains) and intermolecularly (chain redistributions) (2.2-2.3) [73].

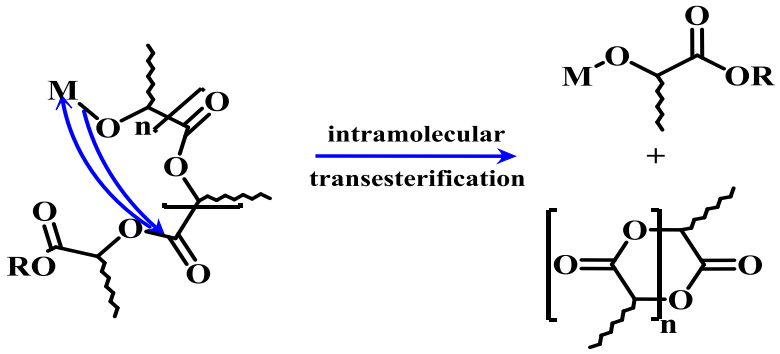
Intermolecular transesterification reactions modify the sequences of copolylactones and prevent the formation of block co-polymers. Intramolecular transesterification reactions cause degradation of the polymer chain and the formation of cyclic oligomers.

The polymerization/depolymerization equilibrium should also be taken into account as a particular case of intramolecular transesterification reaction. All of these side reactions result in broader molecular-weight distributions, sometimes making the molecular weights of the resulting polymers irreproducible. The extent of these undesirable transesterification reactions was found to strongly depend on the metallic initiator [63]. Side reactions occur from the very beginning of the polymerization with $Sn(Oct)_2$, leading to rather broad MWD (PDI indexes around 2) but only at high or even complete conversion with $Al(O\textit{i}\text{-}Pr)_3$, yielding lower PDI indexes (less than 1.5) [63,74].

Parameters that influence the number of transesterifications are temperature, reaction time, and type and concentration of catalyst or initiator. Depending on the metal used, the initiator is more or less active towards transesterification reactions [74].



(2.2)



(2.3)

The promising results obtained with $Sn(Oct)_2$, $Al(O\textit{i}\text{-}Pr)_3$, and $Zn(Lact)_2$ have given rise to a growing interest in metal-based initiators that would display higher catalytic activity and better control the extent of the undesirable transesterification reactions.

Poly(ε-caprolactone)

Poly(ε-caprolactone) (PCL) is a semicrystalline polymer which represents one of several aliphatic polyesters that undergo degradation and absorbtion in vivo [75,76] . The repeating molecular structure of PCL homopolymer consists of five non-polar methylene groups and a single relatively polar ester group. Although not produced from renewable raw materials, PCL is a fully biodegradable thermoplastic polymer due to the presence of the hydrolytically unstable aliphatic-ester linkage. PCL has good water, oil, solvent and chlorine resistance.

PCL has some unusual properties, including a low Tg (~ –60 °C) and Tm (~ 60 °C) and a high thermal stability. These properties are related to PCL's chain of carbons, as longer chains are give rise to less mobility and lower Tm's and Tg's. PCL is also highly permeable, which results from its low Tg and subsequent rubbery state at room temperature.

PCL is one of biodegradable polymers which have been used to prepare functional materials [77]. Copolymers containing poly(ε-caprolactone) (PCL) are especially interesting because they are miscible with a wide range of polymers, and they have features like crystallizability, lack of toxicity, ability to disperse pigments, low-temperature adhesiveness, and printability [78].

PCL has been increasingly studied in the scientific community and applied for drug delivery and tissue engineering [79]. Owing to its high crystallinity and strong hydrophobicity of polymer backbone, PCL homopolymer usually show slow biodegradation and drug-release rate [80].

2.3.3 Cationic Ring-Opening Polymerization

For the ROP of a variety of cyclic heterocycles, cationic polymerization has been applied. the cationic ROP of lactones has been achieved using alkylating agents, acylating agents, Lewis acids, and protic acids.

Early 1970s, it was reportted by Dittrich and Schultz that LA polymerization with cationic compounds were unsuccessfull. In 1986, Kricheldorf and co-workers screened a variety of acidic compounds, among which triflouromethanesulfonic acid (triflic acid, HOTf) and methyl triflate (MeOTf) proved to be useful initiators for cationic ROP of LA [81].

2.3.4 Anionic Ring-Opening Polymerization

The anionic polymerization of lactones with Li or K alkoxides is well-known. However, less work has been done on the anonic ROP of strained heterocycles with organic counterions [81].

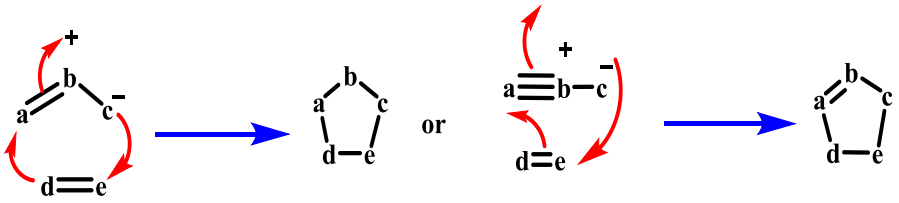
2.4 Click Chemistry

‘Click chemistry’ is a chemical term introduced by Sharpless in 2001 and describes chemistry tailored to generate substances quickly and reliably by joining small units together [82]. Click chemistry can be summarized only one sentence: Molecules that are easy to make. Sharpless also introduced some criteria in order to fullfill the requirements as reactions that: are modular, wide in scope, high yielding, create only inoffensive by-products, are stereospecific, simple to perform and that require benign or easily removed solvent. Nowadays there are several processes have been

identified under this term in order to meet these criterias such as nucleophilic ring opening reactions; non-aldol carbonyl chemistry; thiol additions to carbon–carbon multiple bonds (thiol-ene and thiol-yne); and cycloaddition reactions. Among these selected reactions, copper(I)-catalyzed azide-alkyne (CuAAC) and Diels-Alder (DA) cycloaddition reactions and thiol-ene reactions have gained much interest among the chemists**.**

2.4.1 Copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC)

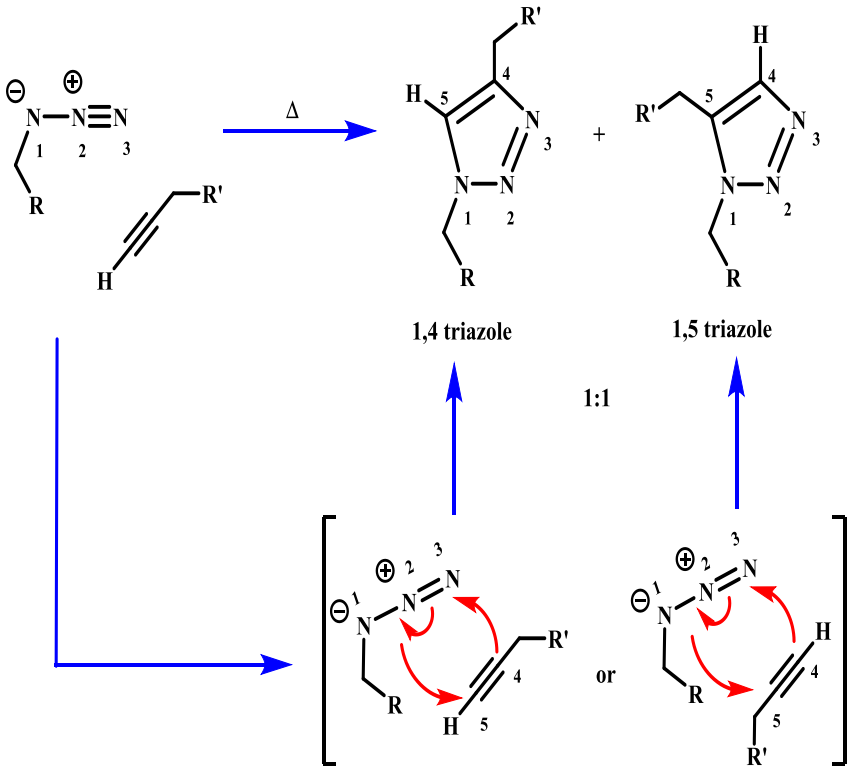
There is a large class of reactions known as 1,3-dipolar cycloaddition reactions (1,3-DPCA) that are analogous to the Diels-Alder reaction in that they are concerted [4π+2π] cycloadditions[83,84]. 1,3-DPCA reactions can be represented as shown in the following diagram. The entity a-b-c is called the *1,3-dipole* and d-e is the *dipolarophile* (2.4).



(2.4)

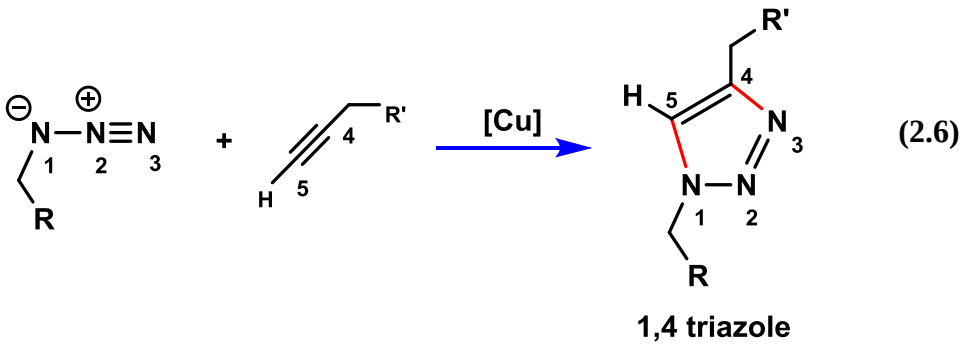
The 1,3-dipoles have a π-electron system consisting of two filled and one empty orbital and are analogous with the allyl or propargyl anion. Each 1,3-dipole has at least one charge-separated resonance structure with opposite charges in a 1,3-relationship. It is this structural feature that leads to the name 1,3-dipole for this class of reactants. The dipolarophiles are typically substituted alkenes or alkynes but all that is essential is a π bond, and other multiply bonded functional groups such as carbonyl, imine, azo, and nitroso can also act as dipolarophiles. The reactivity of dipolarophiles depends both on the substituents present on the π bond and on the nature of the 1,3-dipole involved in the reaction. Owing to the wide range of structures that can serve either as a 1,3-dipole or as a dipolarophile, the 1,3-DPCA is a very useful reaction for the construction of five-membered heterocyclic rings. At this point, a particular interest must be given to Ralf Huisgen for his pionering works on this field (Huisgen 1,3-DPCA)[85]. In his studies, various five-membered heterocyclic rings such as triazole, triazoline, isoxazole, 4-isoxazoline etc. were described. The triazole ring, formed via Huisgen 1,3-DPCA reaction between an azide an alkyne have gained much interest due to its chemically inert character e. g. oxidation, reduction and hydrolysis. The reason behind this fact lies in the inert

character of the two components (azide and alkyne) to biological and organic conditions. Elevated temperatures and long reaction times are important requirements for the triazole formation as stated by Huisgen. Good regioselectivity in the uncatalyzed Huisgen type cycloaddition is observed for coupling reactions involving highly electron-deficient terminal alkynes, but reactions with other alkynes usually afford mixtures of the 1,4- and 1,5-regioisomers (2.5)[86].



(2.5)

Thus, only following the recent discovery of the advantages of Cu(I)-catalyzed alkyne–azide coupling, reported independently by the Sharpless and Meldal groups, did the main benefits of this cycloaddition become clear [86,87]. Cu(I) catalysis dramatically improves regioselectivity to afford the 1,4-regioisomer exclusively (2.6) and increases the reaction rate up to 10^7 times eliminating the need for elevated temperatures[89]. This excellent reaction tolerates a variety of functional groups and affords the 1,2,3-triazole product with minimal work-up and purification, an ideal click reaction[87,88]. Stepwise cycloaddition catalyzed by a monomeric Cu(I) species lowers the activation barrier relative to the uncatalyzed process by as much as 11 kcal/mol, which is sufficient to explain the incredible rate enhancement observed under Cu(I) catalysis.



(2.6)

2.4.2 Diels alder reaction

The Diels-Alder (DA) reaction is a concerted [4π+2π] cycloaddition reaction of a conjugated diene and a dienophile. This reaction is one of the most powerful tools used in the synthesis of important organic molecules. The three double bonds in the two starting materials are converted into two new single bonds and one new double bond to afford cyclohexenes and related compounds (Figure 2.5). This reaction is named for Otto Diels and Kurt Alder, who received the 1950 Nobel prize for discovering this useful transformation [90,92].

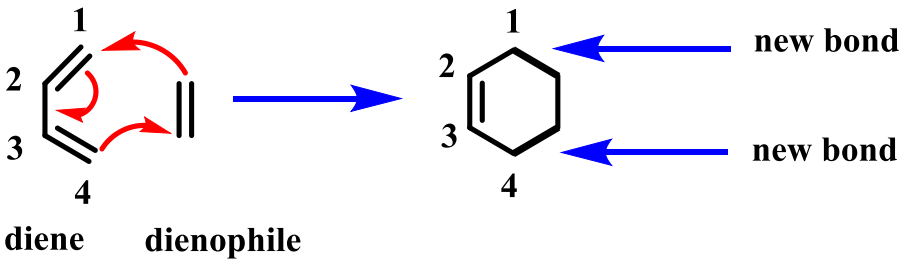


Figure 2.5 : General mechanism of diels-alder [90,92].

Typically, the DA reaction works best when either the diene is substituted with electron donating groups (like -OR, -NR2, etc) or when the dienophile is substituted with electron-withdrawing groups (like -NO2, -CN, -COR, etc)[93].

Stereochemistry of diels alder reaction

There are stereochemical and electronic requirements for the DA reaction to occur smoothly. First, the diene must be in an s-cis conformation instead of an s-trans conformation to allow maximum overlap of the orbitals participating in the reaction (Figure 2.6).

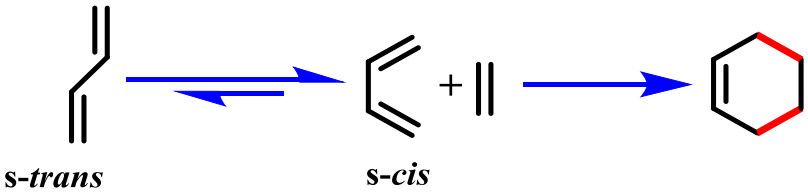


Figure 2.6 : Stereochemistry of diels-alder [94,95].

The "s" in s-cis and s-trans refers to "sigma", and these labels describe the arrangement of the double bonds around the central sigma bond of a diene. Dienes often exist primarily in the lower energy s-trans conformation, but the two conformations are in equilibrium with each other. The s-cis conformation is able to react in the DA reaction and the equilibrium position shifts towards the s-cis conformer to replenish it. Over time, all the s-trans conformer is converted to the s-cis conformer as the reaction proceeds .

A unique type of stereoselectivity is observed in DA reactions when the diene is cyclic. In the reaction of maleic anhydride with cyclopentadiene, for example, the endo isomer is formed (the substituents from the dienophile point to the larger bridge) rather than the exo isomer (the substituents from the dienophile point away from the larger bridge) (Figure 2.7).

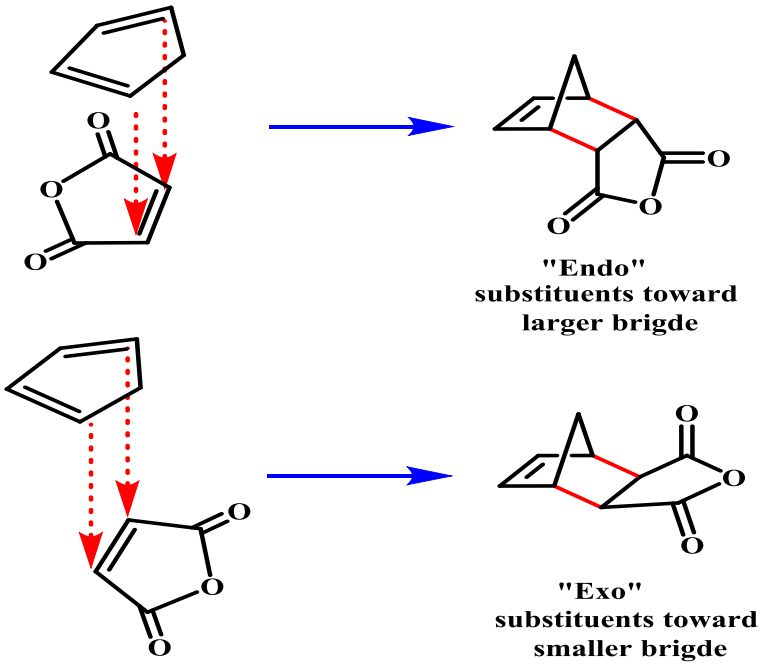


Figure 2.7 : Endo and exo izomers [94,95].

The preference for endo–stereochemistry is "observed" in most DA reactions. The fact that the more hindered endo product is formed puzzled scientists until Woodward, Hoffmann, and Fukui used molecular orbital theory to explain that overlap of the p orbitals on the substituents on the dienophile with p orbitals on the diene is favorable, helping to bring the two molecules together [94,95].

Oftentimes, even though the endo product is formed initially, an exo isomer will be isolated from a DA reaction. This occurs because the exo isomer, having less steric strain than the endo, is more stable, and because the DA reaction is often reversible under the reaction conditions. In a reversible reaction, the product is formed, reverts to starting material, and forms again many times before being isolated. The more stable the product, the less likely it will be to revert to the starting material. If the reaction is not reversible under the conditions used, the kinetic product will be isolated. However, if the first formed product is not the most stable product and the reaction is reversible under the conditions used, then the most stable product, called the thermodynamic product, will often be isolated.

Hoffmann and Fukui shared the 1981 Nobel Prize in chemistry for their molecular orbital explanation of this and other organic reactions. In the illustration below, notice the favorable overlap (matching light or dark lobes) of the diene and the substituent on the dienophile in the formation of the endo product (Figure 2.8):

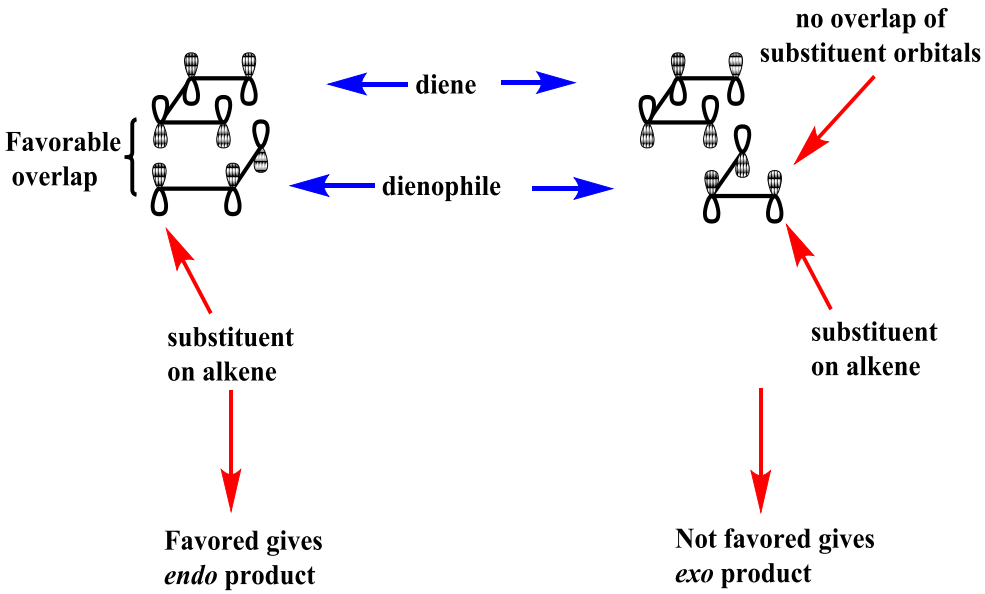
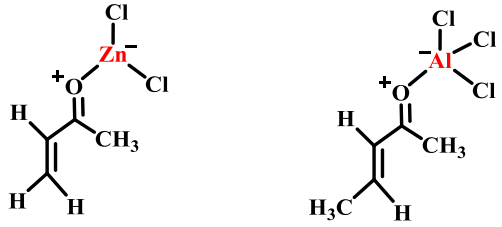


Figure 2.8 : Favorable overlap of the diene and the substituent on the dienophile in the formation of the endo product

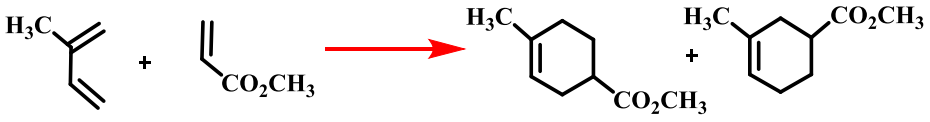
Catalysis of Diels-Alder reactions by Lewis acids

The DA reactions are catalyzed by many Lewis acids, including $SnCl_4$, $ZnCl_2$, $AlCl_3$ and derivatives of $AlCl_3$ [43]. A variety of other Lewis acids is effective catalysts. The types of dienophiles that are subject to catalysis are typically those with carbonyl substituents. Lewis acids form complexes at the carbonyl oxygen and this increases the electron-withdrawing capacity of the carbonyl group (2.9) [96].



(2.9)

This complexation accentuates both the energy and orbital distortion effects of the substituent and enhances both the reactivity and selectivity of the dienophile relative to the uncomplexed compound [97]. Usually, both regioselectivity and *exo*, *endo* stereoselectivity increases. Part of this may be due to the lower reaction temperature. The catalysts also shift the reaction toward a higher degree of charge transfer by making the electron-withdrawing substituent more electrophilic (2.10).



	"para"	"meta"
Uncatalyzed reaction, 120 °C, 6h	**70%**	**30%**
$AlCl_3$-catalyzed 20 °C, 3h	**95%**	**5%**

(2.10)

The solvent also has an important effect on the rate of DA reactions. The traditional solvents were nonpolar organic solvents such as aromatic hydrocarbons. However, water and other polar solvents, such as ethylene glycol and formamide, accelerate a number of DA reactions [98-101]. The accelerating effect of water is attributed to "enforced hydrophobic interactions" [99]. That is, the strong hydrogen bonding network in water tends to exclude nonpolar solutes and forces them together, resulting in higher effective concentrations.

3. EXPERIMENTAL WORK

3.1 Materials

9-anthracene methanol (97%, Aldrich), triethylamine (Et_3N, 99.5%, Aldrich), *N,N'*-dicyclohexylcarbodiimide (DCC, 99 %, Aldrich), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 99%, Aldrich),succinicanhydride (97%, Aldrich), furan (99%, Aldrich), maleic anhydride (99%, Aldrich), ethanolamine (99.5%, Aldrich), 1,4-dioxane (99.8%, Aldrich), 4-dimethyl amino pyridine (DMAP, 99 %, Acros), CuBr (99.9%, Aldrich) 2,2-bis(hydroxymethyl) propionic acid (97%, Acros), *p*-toluenesulfonic acid monohydrate (98.5%, Sigma-Aldrich), 2,2-dimethoxypropane (98%, Sigma-Aldrich), ethyl chloroformate (98%, Fluka), acetone (99.8% for HPLC, Sigma-Aldrich), Toluene (99.5%, Sigma-Aldrich), were used as received. ε-Caprolactone (ε-CL, 99%, Aldrich) was distilled from CaH_2 under vacuum. *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDETA, Aldrich) was destilled over NaOH prior to use. Poly(ethylene glycol monomethyl ether) (PEG-OH) (*M*n= 550 g/mol, Acros) was dried over anhydrous toluene by azeotropic distillation. Dichloromethane (CH_2Cl_2, 99.9 %, Aldrich) was used after distillation over P_2O_5. Tetrahydrofuran (THF, 99.8 %, J.T. Baker) was dried and distilled. Solvents unless specified here were purified by conventional procedures. All other reagents were purchased from Aldrich and used as received without further purification.

3.2 Instrumentation

^1H NMR spectrum were recorded on an Agilent VNMRS 500 (500 MHz for proton and 125 MHz for carbon). The conventional gel permeation chromatography (GPC) measurements were carried out with an Agilent instrument (Model 1100) consisting of a pump, refractive index (RI), and ultraviolet (UV) detectors and four Waters Styragel columns (guard, HR 5E, HR 4E, HR 3, and HR 2), (4.6 mm internal diameter, 300 mm length, packed with 5 μm particles). The effective molecular weight ranges are 2000-4,000,000, 50-100,000, 500-30,000, and 500-20,000,

respectively. THF and toluene were used as eluent at a flow rate of 0.3 mL/min at 30 °C and as an internal standard, respectively. The apparent molecular weights ($_{Mn,GPC}$ and $M_{w,GPC}$) and polydispersities (M_w/M_n) were determined with a calibration based on linear PS standards using PL Caliber Software from Polymer Laboratories.

3.3 Synthetic Procedure

4,10-Dioxatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione **(1)**, 4-(2-hydroxyethyl)-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione **(2)**, 4-(2-(1,3-dioxo-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindol-2(3H)-yl)ethoxy)-4-oxobutanoic acid **(3)**, 1-(3,5-bis(trifloromethyl)phenyl)-3-cyclohexylthiourea **(4)**, 2,2,5-trimethyl-[1,3]dioxane-5-carboxylic acid **(5)**, anthracen-9-ylmethyl 2,2,5-trimethyl-[1,3]dioxane-5-carboxylate **(6)**, anthracen-9-ylmethyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate **(7)**, anthracen-9-ylmethyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate **(8)**, 2-azidoethan-1-ol **(9)**, 2-azidoethyl 2,2,5-trimethyl-1,3-dioxane-5-carboxylate **(10)**, 2-azidoethyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate **(11)**, 2-azidoethyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate **(12)**, furan-protected maleimide-end-functionalized PEG (PEG_{550}-MI) **(13)**, alkyne end-functionalized PCL (Alkyne-PCL) **(14)**, anthracene and azide functionalized polycarbonate (PC-azide-*co*-anth) **(15)**, Copper catalyzed azide-alkyne cycloaddition (CuAAC) reaction between PC-azide-*co*-anth **(16)**, Diels-Alder click reaction between PC-*g*-PCL and PEG_{550}-MI **(17).**

3.3.1 Synthesis of 4,10-dioxatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione (1)

Maleic anhydride (30 g, 0.30 mol) was suspended in 150 mL of toluene and the mixture warmed to 80 °C. Furan (33.4 mL, 0.45 mol) was added via syringe and the turbid solution stirred for 6 h. The mixture was then cooled to ambient temperature white solids formed during standing were collected by filtration and washed with 2 × 30 mL of petroleum ether and once with diethyl ether (50 mL) yielding **1** as white needless. (Yield= 44.4 g, 87%). Mp: 114-115 ^{o}C (DSC). ^{1}H NMR ($CDCl_3$, δ) 6.57 (s, 2H, C*H*=C*H*, bridge protons), 5.45 (s, 2H, -C*H*O, bridge-head protons), 3.17 (s, 2H, C*H*-C*H*, bridge protons). ^{13}C NMR ($CDCl_3$, δ) 170.18, 137.29, 82.46, 48.88. Mass spectrometry (+EI) *m*/*z* (%): 167 [MH+] (50), 144 (35), 130 (20).

3.3.2 Synthesis of 4-(2-hydroxyethyl)-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione (2)

The adduct **1** (10 g, 60 mmol) was suspended in methanol (150 mL) and the mixture was cooled to 0 °C. A solution of ethanolamine (3.6 mL, 60 mmol) in 30 mL of methanol was added dropwise (10 min) to the reaction mixture.

And the resulting solution was stirred for 5 min at 0 °C, then 30 min at ambient temperature, and finally refluxed for 8 h. After cooling the mixture to ambient temperature, solvent was removed under reduced pressure, and residue was dissolved in 150 mL of CH_2Cl_2 and washed with 3 × 100 mL of water. The organic layer was separated, dried over Na_2SO_4 and filtered. Removal of the solvent under reduced pressure gave white-off solid which was further purified by flash chromatography eluting with ethylacetate (EtOAc) to give the product as a white solid. (Yield= 4.9 g, 40%). Mp = 138-139 °C (DSC). ^{1}H NMR ($CDCl_3$, δ) 6.51 (s, 2H, C*H*=C*H*, bridge protons), 5.26 (s, 2H, -C*H*O, bridge-head protons), 3.74-3.68 (m, 4H, NC*H*2C*H*2OH), 2.88 (s, 2H, C*H*-C*H*, bridge protons). 13C NMR ($CDCl_3$, δ) 177.03, 136.60, 81.09, 60.53, 47.74, 42.03. Mass spectrometry (+EI) *m*/*z* (%): 210 [MH+] (50), 145 (22), 142 (100), 124 (17).

3.3.3 4-(2-(1,3-dioxo-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindol-2(3H)-yl)ethoxy)-4-oxobutanoic acid (3)

2 (5 g, 23.9 mmol) was dissolved in 150 mL of 1,4-dioxane. To the reaction mixture were added Et_3N (16.58 mL, 119.6 mmol), DMAP (4.38 g, 35.8 mmol), and succinic anhydride (9.56 g, 95.6 mmol) in that order.

The reaction mixture was stirred for overnight at 50 ^{o}C, then poured into ice-cold water and extracted with CH_2Cl_2. The organic phase was washed with 1 M HCl, dried over Na_2SO_4 and concentrated. The crude product was crystallized from ethanol to give **3** as white crystal. Yield: 5.9 g (80%). M.p. = 122-123 oC (DSC). 1H NMR (CDCl3, δ) 6.50 (s, 2H, C*H*=C*H*, bridge protons), 5.25 (s, 2H, -C*H*O, bridge-head protons), 4.25 (t, *J* = 5.2 Hz, 2H, NCH2C*H*2OC=O), 3.74 (t, *J* =5.2 Hz, 2H, NC*H*2CH2OC=O), 2.87 (s, 2H, C*H*-C*H*, bridge protons), 2.66-2.53 (m, 4H, C=OC*H*2C*H*2C=OOH). 13C NMR (CDCl3, δ) 177.26, 176.35, 172.01, 136.83, 81.09, 61.22, 47.74, 37.92, 29.24. Mass spectrometry (+EI) *m*/*z* (%): 310 [MH+] (100), 242 (100), 142 (18), 124 (13).

3.3.4 1-(3,5-bis(trifloromethyl)phenyl)-3-cyclohexylthiourea) (4)

Cyclohexylamine (1.85 g, 18.5 mmol) was added dropwise at room temperature to a stirring solution of 3,5-bis(trifluoromethyl)phenyl isothiocyanate (5.0 g, 19 mmol) in THF (20 mL). After the solution was stirred for 4 h, the solvent was evaporated. The white residue was recrystallized from hexane to give TU as a white powder. Yield: 5.90 g (86%). ^{1}H NMR (500 MHz, CDCl3, δ) 7.71 (s, 1H, 4-Ar*H*), 7.75 (s, 2H, 2,6-Ar*H*), 6.13 (s, 1H, CyN*H*), 4.20 (br 1H, NCy*H*), 2.06-1.21 (10H, Cy(*H2*)5).

3.3.5 Synthesis of 2,2,5-trimethyl-[1,3]dioxane-5-carboxylic acid (5)

The 2,2-bis(hydroxymethyl)propanoic acid (16 g, 119.2 mmol) along with *p*-TSA (0.9 g, 4.64 mmol), and 2,2-dimethoxypropane (22.4 mL, 178.8 mmol) dissolved in 80 mL of dry acetone, and stirred 2 h at room temperature. In the vicinity of 2 h, while stirring continued the reaction mixture was neutralized with 12 mL of totally NH_4OH (25%), and absolute ethanol (1:5), filtered off by-products and subsequent dilution with dichloromethane (240 mL), and once extracted with distilled water (80 mL). The organic phase dried with Na_2SO_4, concantrated to yield 14.8 g (71%) as white solid after evaporation of the solvent. ^{1}H NMR ($CDCl_3$, δ) 4.18 (d, 2H, CC*H*$_2$O), 3.63 (d, 2H, CC*H*$_2$O), 1.38 (s, 3H, C*CH*$_3$) 1.36 (s, 3H, C*CH*$_3$), 1.18 (s, 3H, C=OC(CH_2O)$_2$*CH*$_3$).

3.3.6 Synthesis of anthracen-9-ylmethyl 2,2,5-trimethyl-[1,3]dioxane-5-carboxylate (6)

9-Anthracene methanol(6.5 g, 31.25 mmol) was dissolved in 100 mL of CH_2Cl_2 and **5** (6.5 g, 37.4 mmol), and DMAP (5.5 g, 45.13 mmol) were added to the reaction mixture in that order. After stirring 5 minutes at room temperature, DCC (9.25 g, 44.9 mmol) dissolved in 50 mL of CH_2Cl_2 was added. Reaction mixture was stirred overnight at room temperature and urea byproduct was filtered. Solvent was evaporated and the remaining product was purified by column chromatography over silica gel eluting with hexane/dichlorometane (4:1) to give pale yellow oil (Yield = 9.22 g; 81 %). ^{1}H NMR (CDCl3, δ) 8.50 (s, 1H, Ar*H* of anthracene), 8.32 (d, 2H, Ar*H* of anthracene), 8.02 (d, 2H, Ar*H* of anthracene), 7.60-7.45 (m, 4H, Ar*H* of anthracene), 6.2 (s, 2H, *CH*$_2$-anthracene), 4.14 (d, 2H, CC*H*$_2$O), 3.58 (d, 2H, CC*H*$_2$O), 1.38 (s, 3H, C*CH*$_3$), 1.35 (s, 3H, C*CH*$_3$), 1.08 (s, 3H, C=OC(CH_2O)2*CH*$_3$).

3.3.7 Synthesis of anthracen-9-ylmethyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate (7)

9-anthrylmethyl 2,2,5-trimethyl-1,3-dioxane-5-carboxylate (9.22 g, 25.3 mmol) was dissolved in a mixture of 100 mL of THF and 100 mL of 1 M HCl. The reaction mixture was stirred for 2 h at room temperature. The precipitated product was filtered off and reaction mixture was concentrated and extracted with 480 mL of CH_2Cl_2 and 80 mL of water. The combined organic phase was dried with Na_2SO_4 and concentrated. Hexane was added to the reaction mixture and it was kept in deep freeze overnight to give white solid (Yield = 8.2 g, 89 %). 1H NMR (CDCl3, δ) 8.52 (s, 1H, Ar*H* of anthracene), 8.30 (d, 2H, Ar*H* of anthracene), 8.03 (d, 2H, Ar*H* of anthracene), 7.60-7.45 (m, 4H, Ar*H* of anthracene), 6.2 (s, 2H, *CH*$_2$-anthracene), 3.85 (d, 2H, C*H*$_2$OH), 3.66 (d, 2H, C*H*$_2$OH), 2.17(br, 2H, OH), 1.01 (s, 3H, C*CH*$_3$).

3.3.8 Synthesis of anthracen-9-ylmethyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate (8)

In a 250 mL of three-neck round bottom flask were added **7** (8.2 g, 25.5 mmol) in100 mL of THF. The solution was cooled to 0 °C, and a solution of ethyl chloroformate (4.82 mL,44 mmol) in 25 mL of THF was added dropwise to the reaction mixture. Then a solution of triethylamine (10.56 mL, 10.5 mmol) in 25 mL of THF was added dropwise (20 min). The white suspension was stirred for 2 h at 0°C and subsequently at ambient temperature for overnight. The ammonium salt was filtered off and the solvent was removed under reduced pressure to give a yellow residue that was further purified by crystallization from dry THF to give white powder. Yield: 6.8 g (83%). ^{1}H NMR ($CDCl_3$, δ) 8.56 (s, 1H, Ar*H* of anthracene), 8.26 (d, 2H, Ar*H* of anthracene), 8.07 (d, 2H, Ar*H* of anthracene), 7.60-7.54 (m, 4H, Ar*H* of anthracene), 6.28 (s, 2H, C*H*$_2$-anthracene), 4.65 (d, 2H, CC*H*$_2$OC=O), 4.15 (d, 2H, CC*H*$_2$OC=O), 1.24 (s, 3H, C=OC(CH2O)$_2$*CH*$_3$).

3.3.9 Synthesis of 2-azidoethan-1-ol (9)

2-Bromoethanol (10.0 g 80.0 mmol) was dissolved in 120 mL of acetone. NaN_3 (7.80 g, 120 mmol) in 30 mL of water was added to the reaction mixture. The white suspension was stirred and refluxed in the oil bath at 60°C for overnight. Solvent was evaporated at 40°C and the reaction mixture was residue was dissolved in 150 mL of

CH_2Cl_2 and washed with 3 × 100 mL of water. The organic layer was separated, dried over Na_2SO_4 and filtered to give viscous clear oil. Yield: 3.71 g (53%).

3.3.10 Synthesis of 2-azidoethyl 2,2,5-trimethyl-1,3-dioxane-5-carboxylate (10)

2-azidoethan-1-ol (3,71 g, 42.64 mmol) was dissolved in 100 mL of CH_2Cl_2 and **5** (8,16 g, 46.9 mmol), and DMAP (2.59 g, 21.23 mmol) were added to the reaction mixture in that order. After stirring 5 minutes at room temperature, DCC (9.7 g, 46.86 mmol) dissolved in 50 mL of CH_2Cl_2 was added. Reaction mixture was stirred overnight at room temperature and urea byproduct was filtered. Solvent was evaporated and the remaining product was purified by column chromatography over silica gel eluting with firstly 300 mL of hexane to seperate than impurity and then hexane/ ethylacetate (4:1). Hexane was added to the reaction mixture and it was kept in deep freeze overnight to give viscous clear oil. Yield: 4.19 g (40%). ^{1}H NMR ($CDCl_3$, δ) 4.21 (d, 2H, CC*H*$_2$O), 3.69 (d, 2H, CC*H*$_2$O), 1.40 (s, 3H, C*CH*$_3$) 1.44 (s, 3H, C*CH*$_3$), 1.22 (s, 3H, C=OC(CH_2O)$_2$*CH*$_3$), 4.32 (t, 2H, CC*H*$_2$O), 3.50 (t, 2H, CC*H*$_2$N).

3.3.11 Synthesis of 2-azidoethyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate (11)

2-azidoethyl 2,2,5-trimethyl-1,3-dioxane-5-carboxylate (4.19 g, 17.22 mmol) was dissolved in a mixture of 45 mL of THF and 45 mL of 1 M HCl. The reaction mixture was stirred for 2 h at room temperature. The precipitated product was filtered off and reaction mixture was concentrated and extracted with 480 mL of CH_2Cl_2 and 80 mL of water. The combined organic phase was dried with Na_2SO_4 and concentrated to give viscous yellow oil. Yield: 2.61 g (75%). ^{1}H NMR ($CDCl_3$, δ) 3.93 (d, 2H, CC*H*$_2$O), 3.77 (d, 2H, CC*H*$_2$O), 1.11 (s, 3H, C=OC(CH_2O)$_2$*CH*$_3$), 4.34 (t, 2H, CC*H*$_2$O), 3.51 (t, 2H, CC*H*$_2$N).

3.3.12 Synthesis of 2-azidoethyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate (12)

In a 250 mL of three-neck round bottom flask were added **11** (2.61 g, 12.84 mmol) in 100 mL of THF. The solution was cooled to 0 °C, and a solution of ethyl chloroformate (3.54 mL, 37.44 mmol) in 25 mL of THF was added dropwise to the reaction mixture. Then a solution of triethylamine (7.76 mL, 56.15 mmol) in 25 mL of THF was added dropwise (20 min). The suspension was stirred for 2 h at 0°C and subsequently at ambient temperature for overnight. The ammonium salt was filtered

off and the solvent was removed under reduced pressure to give a yellow residue that was further purified by crystallization from diethyelether to give viscous brown oil. Yield: 1.8 g (61%). ^{1}H NMR ($CDCl_3$, δ) 4.72 (d, 2H, CC*H*$_2$O), 4.24 (d, 2H, CC*H*$_2$O), 1.38 (s, 3H, C=OC(CH$_2$O)$_2$*CH*$_3$), 4.39 (t, 2H, CC*H*$_2$O), 3.54 (t, 2H, CC*H*$_2$N).

3.3.13 Preparation of furan-protected maleimide-end-functionalized PEG (PEG-MI) (13)

Me-PEG$_{11}$ (*M*n = 550) (2.0 g, 3.63 mmol) was dissolved in 50 mL of CH_2Cl_2. To the reaction mixture were added DMAP (0.044 g, 0.363 mmol) and **3** (2.24 g, 7.27 mmol) in that order. After stirring 5 min at room temperature, a solution of DCC (1.49 g, 7.27 mmol) in 10 mL of CH_2Cl_2 was added. Reaction mixture was stirred for overnight at room temperature. After filtration off the salt, the solution was concentrated and the viscous brown color product was purified by column chromatography over silica gel eluting with CH_2Cl_2/EtOAc mixture (1:1, v/v) and then with CH_2Cl_2/methanol (90:10, v/v) to obtain MI-PEG as viscous brown oil. Yield: 2.7 g (88%). ^{1}H NMR ($CDCl_3$, δ) 6.50 (s, 2H, C*H*=C*H* as bridge protons), 5.24 (s, 2H, -C*H*O, bridge-head protons), 4.21 (m, 4H, C*H*2OC=O), 3.74-3.53 (m, OC*H*2C*H*2 repeating unit of PEG, C=ONC*H*2, and C*H*2-PEG repeating unit), 3.36 (s, 3H, PEG-OC*H*3), 2.86 (s, 2H, C*H*-C*H*, bridge protons) 2.61-2.56 (m, 4H, C=OC*H*2C*H*2C=O).

3.3.14 Synthesis of alkyne end-functionalized PCL (Alkyne-PCL) (14)

Alkyne-PCL was prepared by ROP of ε-CL (5.0 mL, 0.047 mol) in bulk using tin(II)-2-ethylhexanoate as a catalyst and propargyl alcohol (0.056 mL, 0.94 mmol) as an initiator at 110 °C for 28 h., The degassed monomer, catalyst, and initiator were added to a previously flamed schlenk tube equipped with a magnetic stirring bar in the order mentioned. The tube was degassed with three FPT, left in argon, and placed in a thermostated oil bath. After the polymerization, the mixture was diluted with THF, and precipitated into an excess amount of cold methanol. It was isolated by filtration and dried at 40 ^{o}C in a vacuum oven for 24 h. ^{1}H NMR ($CDCl_3$, δ) 4.68 (s, 2H, CH≡C-C*H*$_2$O), 4.07 (t, 2H, C*H*$_2$OC=O of PCL), 3.66 (t, 2H, C*H*$_2$OH, end-group of PCL), 2.48 (t, 1H, C*H*≡C-CH$_2$O), 2.31 (t, 2H, C=OC*H*$_2$ of PCL), 1.3-1.7 (m, 6H, C*H*$_2$ of PCL).

3.3.15 Preparation of pendant anthracene and azide functionalized polycarbonate (PC-azide-*co*-anth) (15)

PC-azide-*co*-anth was prepared by ROP of Ant-Carbonate (0.5 g, 1.42 mmol) and Azide-Carbonate (0.32 g, 0.14 mmol) using both DBU (0.021 mL, 0.14 mmol) and **4** (0.053 g, 0.14 mmol) as catalyst and benzyl alcohol (0.015 mL, 0.14 mmol) as an initiator at room temperature for overnight. The degassed monomer in CH_2Cl_2 (9 mL), catalyst, and initiator were added to a 25 mL 2-neck round bottom flask that had been flame-dried under vacuum and purged with argon. The tube was degassed with three freeze-pump-thaw (FPT) and left in vacumm. After the polymerization, the mixture was concentrated and precipitated into an excess amount of methanol at ambient temperature. Recovered polymer, redissolved in CH_2CL_2 and precipitated in methanol. It was isolated by filtration and dried at 40 ^oC in a vacuum oven for 6 h. ^1H NMR ($CDCl_3$, δ) 8.2 (br, Ar*H* of anthracene), 7.9 (br, Ar*H* of anthracene), 7.48 (bs, Ar*H* of anthracene), 7.4-7.2 (br, Ar*H* of anthracene and Ar*H* of Ph), 6.10 (bs, C*H*2-anthracene), 5.02 (s, 2H, OC*H*2-Ph), 4.19 (bs, C*H*2OC=O of PC and OC*H2*CH2) , 3.37 (bs, NC*H2*CH2), 1.05 (bs, C=OC(CH2O)2*CH3*). $M_{n,theo}$ =5900; $M_{n,GPC}$ =6550, $M_{n,NMR}$ =5300, M_w/M_n =1.395 (relative to PS standards).

3.3.16 Copper catalyzed azide-alkyne cycloaddition (CuAAC) reaction between PC (azide-*co*-anth) and Alkyne-PCL (16)

PC-azide$_7$-anth$_{10}$ (0.4 g, 0.075 mmol, $M_{n,NMR}$=5300, 1 equiv.), **14** (1.86 g, 0.75 mmol $M_{n,NMR}$=2460, 10 equiv.) were dissolved in nitrogen-purged DMF (12 mL) in a Schlenk tube. CuBr (0.076 g, 0.53 mmol) and PMDETA (0.11 mL, 0.53 mmol) were added and the reaction mixture was degassed by three FPT cycles, left in argon, and stirred at room temperature for 12 h. After this specified time, the polymer solution was passed through alumina column to remove copper salt and precipitated in methanol. Subsequently, the crude product was dissolved in THF and precipitated in diethyl ether/methanol (1:4) and subsequently in methanol. Finally, recovered polymer was dried in a vacuum oven at 40 ^oC . Yield = 1.1 g (65 %). ^1H NMR ($CDCl_3$, δ) 8.51-7.45 (m, Ar*H* of anthracene and C*H* of triazole), 6.08 (s, 2H, C*H*2-anthracene), 5.15 (br, 2H, triazole-C*H2* and 2H, OC*H*2-Ph), 4.45 (m, 2H, C*H*2OC=O and OC*H2*CH2), 4.07 (bs, C*H*2O of PCL), 3.65 (br, 2H, CH2C*H*2OH and 2H CH2C*H2*N), 2.31 (s, 2H, CHCH_2=O), 1.66 (s, 2H, O=CH_2CH_2), 1.66-1.39 (m, CH_2 of PCL), 1.09 (m, 6H, CC*H3*).

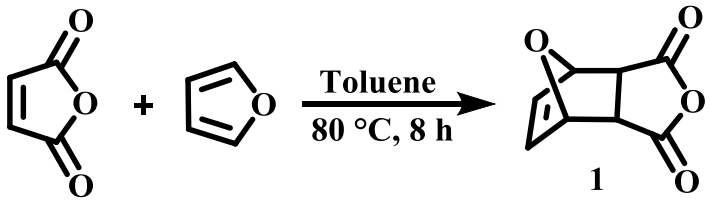
3.3.17 Diels–Alder click reaction of PC-*g*-PCL and PEG_{550}-MI (17)

16 (0.2 g, 0.008 mmol) was dissolved in 40 mL of toluene. **13** (0.08g, 0,1 mmol) and small amount of BHT in 40 mL of toluene was added to the solution. The mixture was bubbled with nitrogen for 30 minutes and refluxed for 40 h at 110 ^{o}C in the dark. After the specified time, solution was evaporated to dryness and the residual solid was dissolved in THF, and subsequently precipitated in methanol. This dissolution-precipitation procedure was repeated two times. The obtained product was dried in a vacuum oven at 40 ^{o}C for 24 h. Yield = 0.18 g (75 %). ^{1}H NMR ($CDCl_3$, δ) %). ^{1}H NMR ($CDCl_3$, δ) 7.41-7.14 (m, Ar*H* of anthracene and C*H* of triazole), 5.50 (s, 2H, C*H*2-anthracene), 5.15 (br, 2H, triazole-C*H2* and 2H, OC*H*2-Ph), 4.23 (br, 2H, C*H*2OC=O and OC*H2*CH2), 4.07 (bs, C*H*2O of PCL), 3.65 (br, 2H, CH2C*H*2OH, 2H CH2C*H2*N and 4H *CH2CH2*O of PEG), 2.31 (s, 2H, CHCH_2=O), 1.66 (s, 2H, O=$CH_2C H_2$), 1.39 (m, CH_2 of PCL), 1.17 (m, 6H, CC*H3*).

4. RESULTS AND DISCUSSION

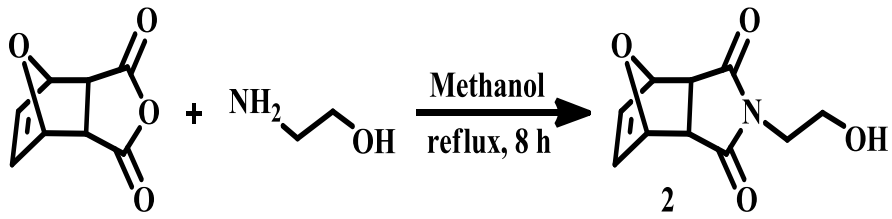
4.1 Synthesis of Initiators

First of all, maleic anhydride and furan were reacted in toluene at reflux temperature for 8 h to give 4,10-Dioxatricyclo[5.2.1.02,6]dec-8-ene-3,5-dione **(1)** (equation 4.1). The anhydride **1** was obtained as small white needless.



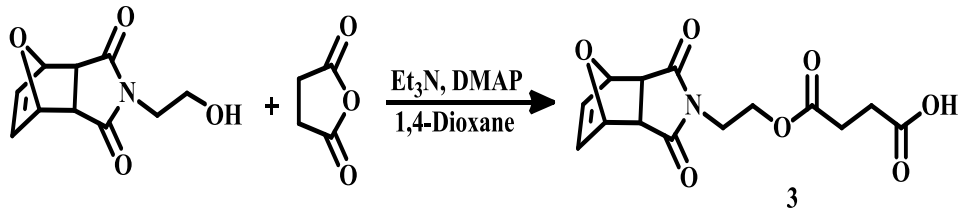
(4.1)

The reaction of the anhydride 4,10-Dioxatricyclo[5.2.1.02,6]dec-8-ene-3,5-dione **(1)** was then carried out to give the 4-(2-Hydroxyethyl)- 10-oxa-4-azatricyclo[5.2.1.02,6]dec-8-ene-3,5- dione **(2).** In this reaction, the anhydride **1** was suspended in MeOH and a solution of ethanolamine in MeOH was added at 0 ^{o}C, then the mixture refluxed for 8 h (4.2). Finally, compound **2** was obtained as a white solid.



(4.2)

The hydoxyl functionality of the 4-(2-Hydroxyethyl)- 10-oxa-4-azatricyclo[5.2.1.02,6]dec-8-ene-3,5- dione **(2)** was converted to carboxylic acid via a reaction with succinic anhydride in the presence of Et_3N/DMAP catalyst system and 1,4-dioxane as solvent in order to give the 4-(2-{[(3-acetyl-7-oxabicyclo[2.2.1]hept-yl)carbonyl]amino}ethoxy)-4-oxobutanoic acid **(3)** (4.3).



(4.3)

From overlay ^{1}H NMR spectra Figure 4.1 of **3**, methylene protons next to the ester ($NCH_2CH_2OC{=}O$) and methylene protons adjacent to nitrogen ($NCH_2CH_2OC{=}O$) appeared at 4.25 ppm and 3.74 ppm respectively. Moreover, the multiplet peaks around 2.66-2.53 ppm confirmed successful conversion of hydroxyl group to carboxylic acid. Moreover, the characteristic protons of the adduct were also detected at 6.49 ppm (bridge vinyl protons), 5.24 ppm (bridge-head protons) and 2.85 ppm (bridge protons) respectively. These results confirmed that the synthesis of **3** was achived.

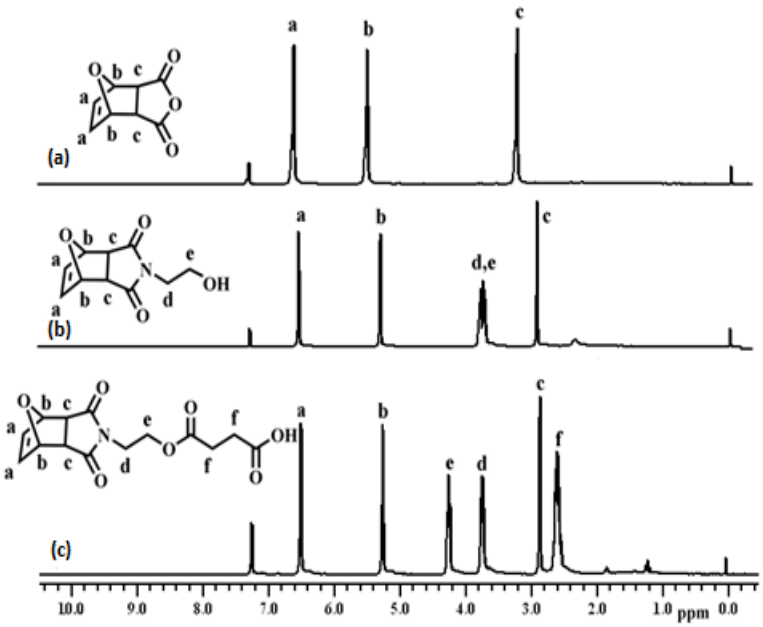
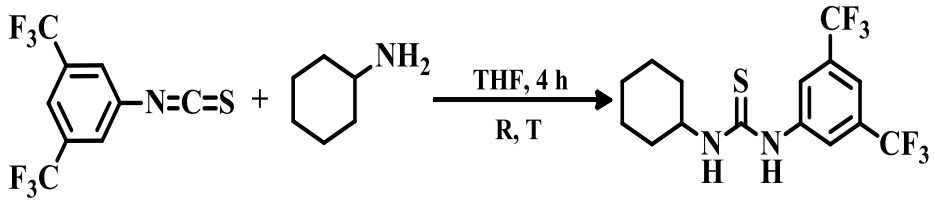


Figure 4.1 : ^{1}H NMR spectra of: **a**) 3-acetyl-N-(2-hydroxyethyl)-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid **(1)**; **b**) 3-acetyl-N-(2-hydroxyethyl)-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxamide (**2)**; **c)** 4-(2-{[(3-acetyl-7-oxabicyclo[2.2.1]hept-yl)carbonyl]amino}ethoxy)-4-oxobutanoic acid **(3)** in $CDCl_3$.

To synthesize 1-(3,5-bis(trifloromethyl)phenyl)-3-cyclohexylthiourea) is in other world co-catalyst (TU), cyclohexylamine and 3,5-bis(trifluoromethyl)phenyl isothiocyanate were reacted in THF at room temperature for 4h (4.4). Finally, compound **4** was obtained as a white solid.



(4.4)

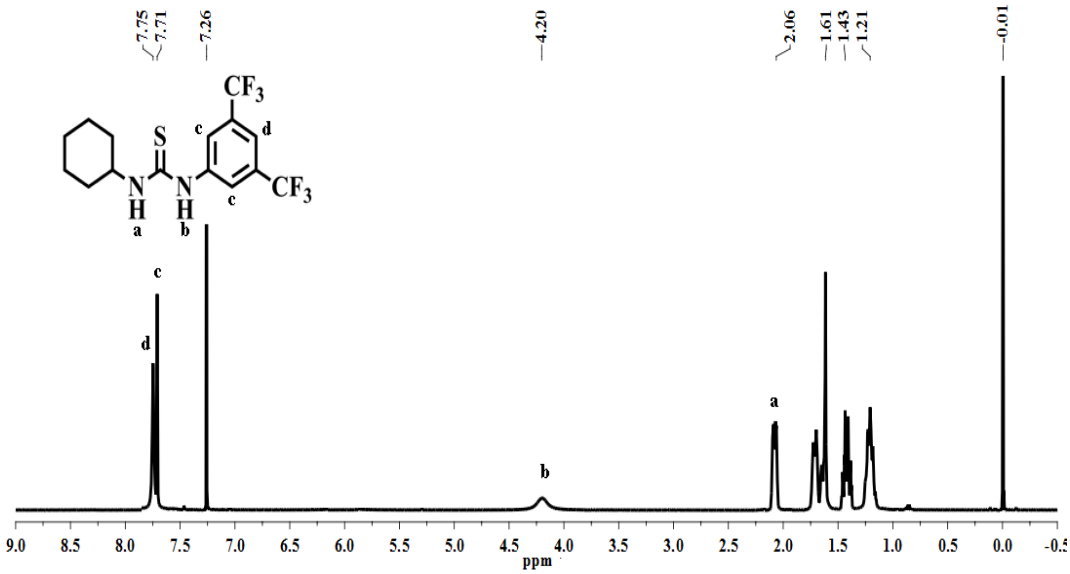
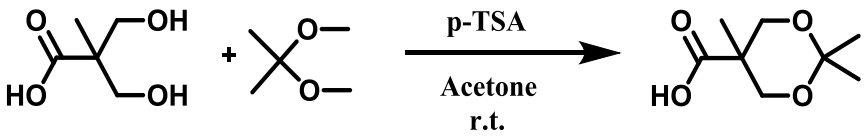


Figure 4.2 : ^{1}H NMR spectrum of 1-(3,5-bis(triflоromethyl)phenyl)-3-cyclohexylthiourea) in $CDCl_3$ (500 MHz).

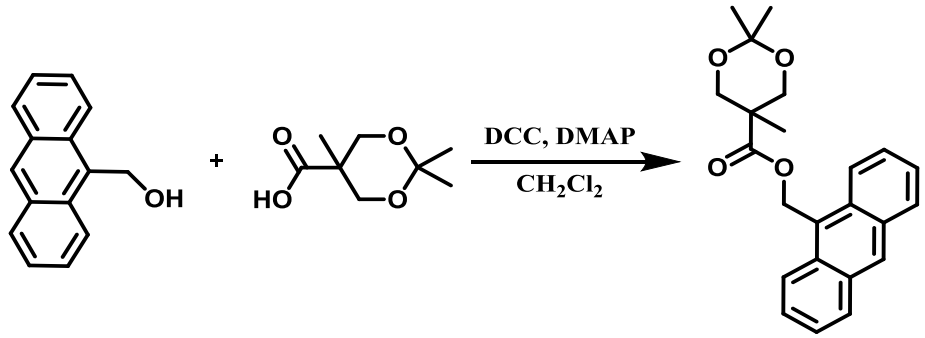
4.2 Preparation of Antracene and Azide Functional Carbonate Monomers

First of all 2,2,5-trimethyl-[1,3]dioxane-5-carboxylic acid **(5)** was synthesized by this way; 2, 2-bis (hydroxymethyl)-propanoic acid was reacted with excess amount of dry acetone using *p*-toluene sulfonic acid as catalyst. Additionally, 2,2-dimethoxy-propane was deliberately used to provide acetone during the reaction. Process is given below schematically (4.5).



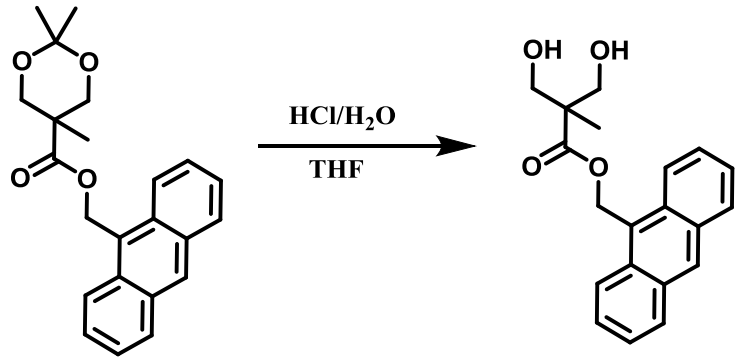
(4.5)

Initially, esterification reaction of anthracen-9-ylmethanol and 2,2,5-trimethyl-1,3-dioxane-5-carboxylic acid was prepared to synthesize **(6)** (anthracen-9-ylmethyl 2,2,5-trimethyl-1,3-dioxane-5-carboxylate) by catalyzing DCC and DMAP in CH_2Cl_2 at room temperature overnight (4.6).



(4.6)

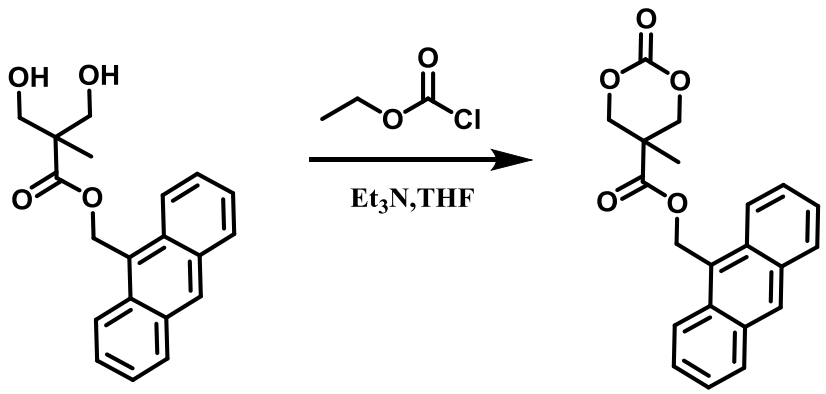
Next, anthracene-9-ylmethyl 2,2,5-trimethyl-1,3-dioxane-5-carboxylate **(6)** was hydrolized in THF by adding HCl solution stirring for 2 hours at room temperature.



(4.7)

Thus, anthracen-9-ylmethyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate **(7)** was obtained. (4.7)

^{1}H NMR spectroscopy confirmed clearly the structure of 10 by appearance of characteristic signals of anthracene (δ 8.5−7.5) . It is obviously seen that the peak of methylene protons neighbouring to hydroxyl group is between 3.63 and 3.85 ppm. In the following step, Anth-carbonate monomer (anthracen-9-ylmethyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate) was synthesized (4.8). The cyclization was performed in the presence of ethyl chloroformate in dilute anhydrous THF solution via dropwise addition of triethylamine.



(4.8)

^{1}H NMR spectroscopy confirmed clearly the structure of **6** by appearance of characteristic signals of anthracene (δ8.5-7.5). The double doublets at δ 4.15/4.65 were attiributable to the methylene protons next to the carbonate. Importantly, no peak at δ 3.63-3.85 assignable to the methylene protons adjacent to the hydroxyl group was detected. The ^{1}H NMR and elemental analysis of Anth-carbonate showed similar outcome.

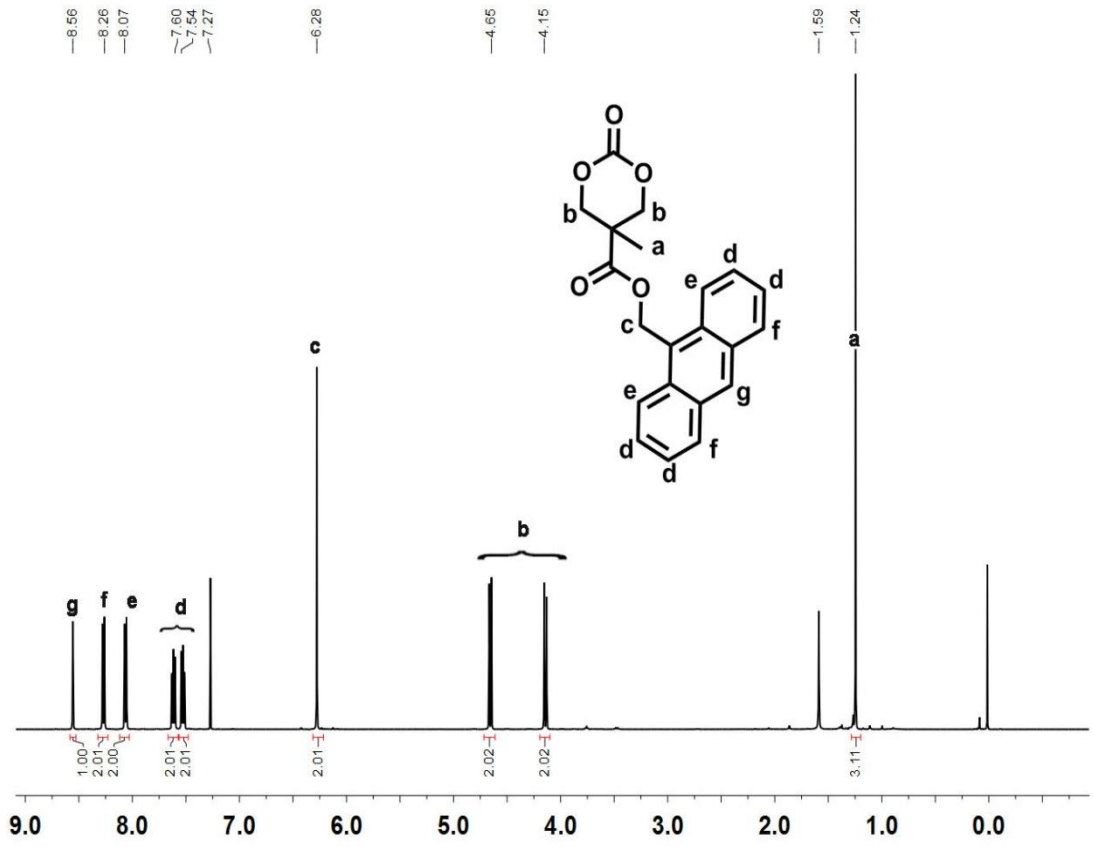
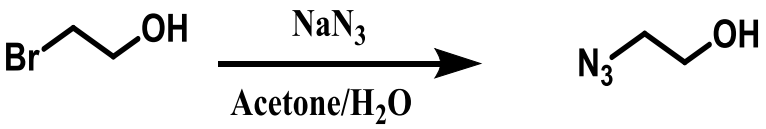


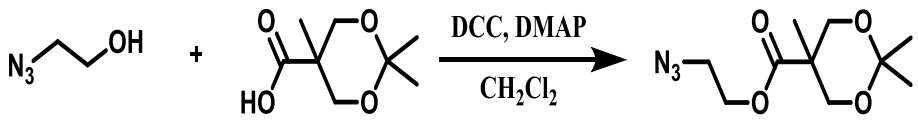
Figure 4.3 : ^{1}H NMR spectrum of Anth-Carbonate in $CDCl_3$ (500 MHz).

Synthesis of 2-azidoethan-1-ol **(9)** was synthesized by this way; 2-Bromoethanol was reacted with NaN_3 in acetone at 60 ^oC (4.9).



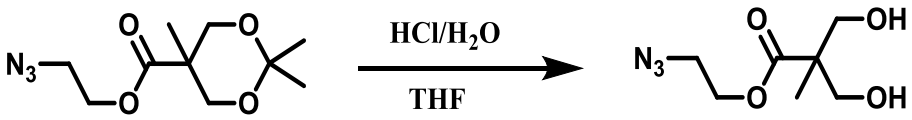
(4.9)

Then esterification reaction of 2-azidoethan-1-ol and 2,2,5-trimethyl-1,3-dioxane-5-carboxylic acid was prepared to synthesize 2-azidoethyl 2,2,5-trimethyl-1,3-dioxane-5-carboxylate **(10)** by catalyzing DCC and DMAP in CH_2Cl_2 at room temperature overnight (4.10).



(4.10)

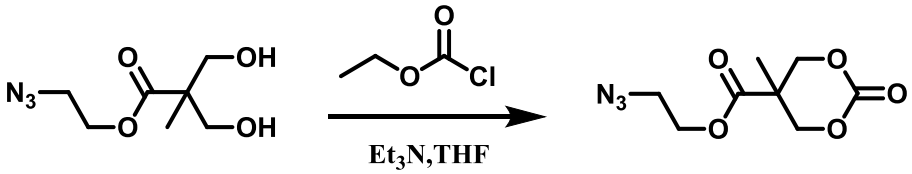
Next, 2-azidoethyl 2,2,5-trimethyl-1,3-dioxane-5-carboxylate **(10)** was hydrolized in THF by adding HCl solution stirring for 2 hours at room temperature.



(4.11)

Thus, was obtained 2-azidoethyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate **(11)** (4.11).

In the following step, azide-carbonate monomer (2-azidoethyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate) was synthesized (4.12). The cyclization was performed in the presence of ethyl chloroformate in dilute anhydrous THF solution via dropwise addition of triethylamine.



(4.12)

^{1}H NMR spectroscopy confirmed clearly the structure of 2-azidoethyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate by appearance of characteristic signals of protons (δ 4.39-3.54).

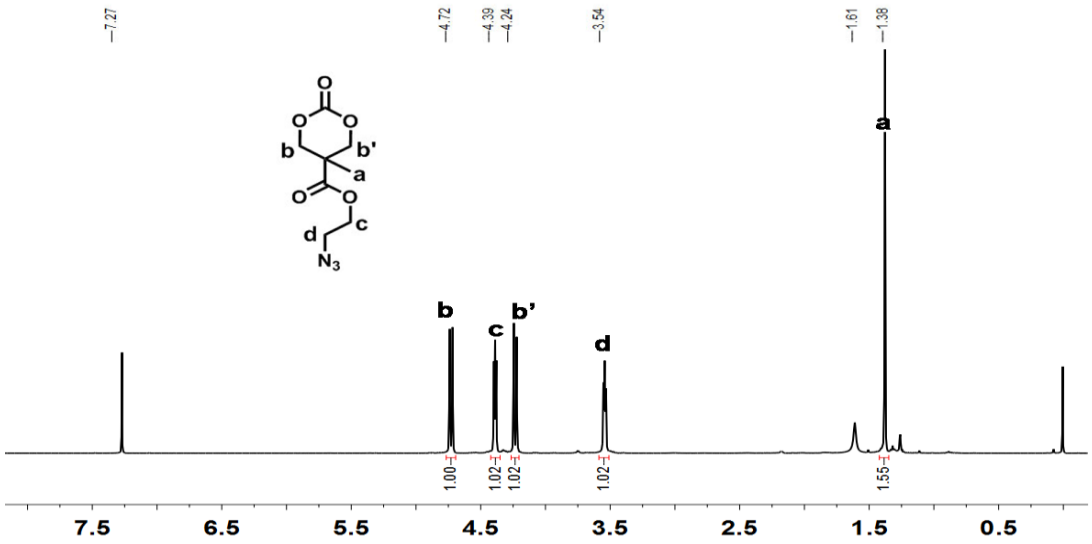


Figure 4.4 : ^{1}H NMR spectrum of Azide-Carbonate in $CDCl_3$ (500 MHz).

4.3 Preparation of anthracene and azide functional polycarbonate (PC- azide-*co*-anth)

The benzyl-terminated polycarbonate was prepared from the ROP of anthracene-9-ylmethyl 2,2,5-trimethyl-1,3-dioxane-5-carboxylate (**8**) and 2-azidoethyl 5-methyl-2-oxo-1,3-dioxane-5 **(12)** using benzyl alcohol as initiator and TU/DBU as catalyst in CH_2Cl_2 at room temperature for 24 h. The structure of the PC was confirmed by ^1H NMR.

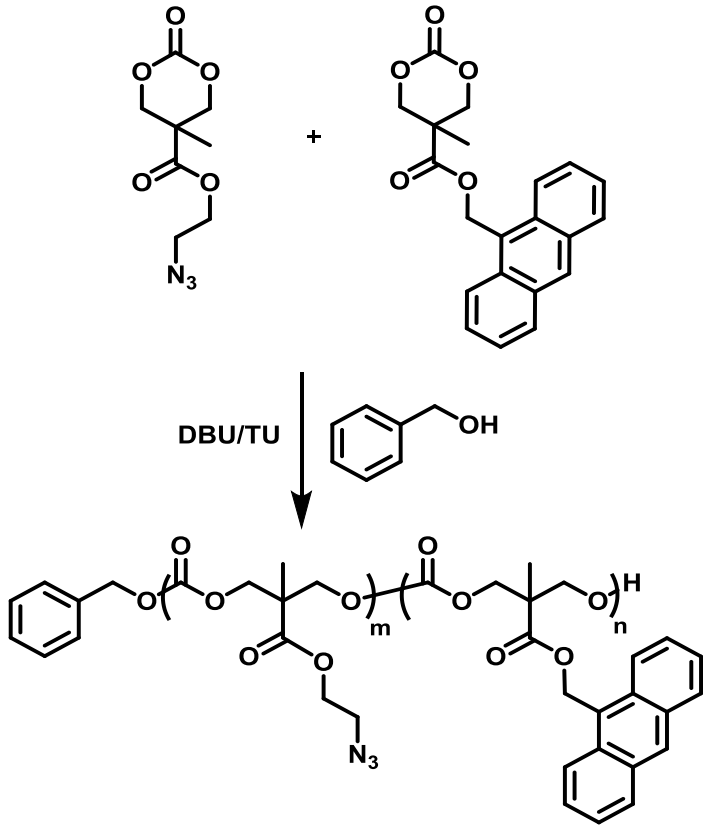


Figure 4.5 : ROP of Anthracene and Azide Functional Carbonate Monomers

Anth carbonate, azide carbonate, initator and DBU, TU ratio was 10:10:1:1:1, respectively. DCM used as the solvent and volume of the solvent was around 10 mL. 30 ^oC oil bath was prepared for the reaction. Polymerization was carried out successfully under these conditions and ^1H NMR spectrum (Figure 4.6) and GPC data (Figure 4.12) confirmed the structure. From ^1H NMR spectroscopy, two doublets (4.65 and 4.15 ppm) corresponding to the CH_2 adjacent to the carbonate group disappeared and a new broad singlet signal at 4.19 ppm that is assigned to the CH_2OC=O of PC appeared in association with the characteristic signals of the anthracene and CH_2 linked to the anthracene at 8.20-7.90 and 7.46 ppm, respectively.

The number-average molecular weight ($M_{n,NMR}$ = 10 (*DP*n) X 350 g/mol + 7(*DP*n) X 230 g/mol MW of end-groups (108 g/mol) = 5300 g/mol) of the PC-azide$_7$-*co*-anth$_{10}$ could be calculated by comparing integrated signals of the main backbone.

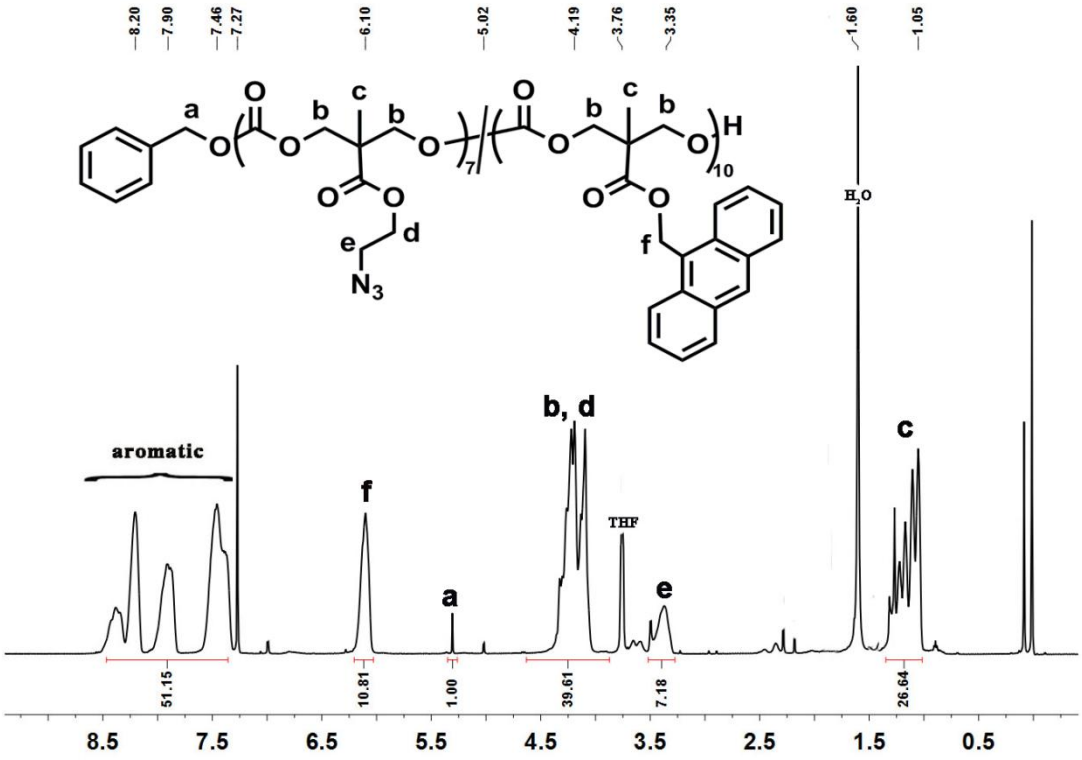
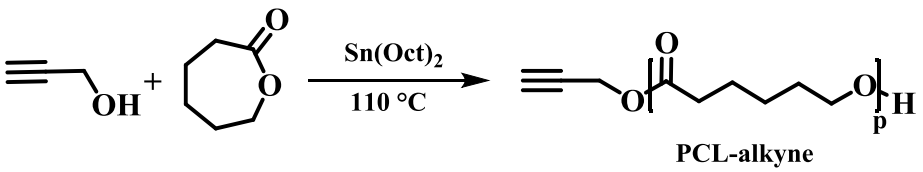


Figure 4.6 : ^{1}H-NMR spectrum of PC(anth-*co*-azide) in $CDCl_3$ (500 MHz).

4.4 Sequential Copper catalyzed azide-alkyne cycloaddition (CuAAC) of Alkyne-PCL and Diels-Alder Click reaction of MI-PEG on PC(azide$_7$-*co*-anth$_{10}$)

4.4.1 Copper catalyzed azide-alkyne cycloaddition (CuAAC) reaction between PC-azide-*co*-anth) and Alkyne-PCL

The PCL-alkyne was obtained by ROP of ε-CL in bulk using tin(II) 2-ethylhexanoate, $Sn(Oct)_2$ as a catalyst and propargyl alcohol as an initiator (4.15).



(4.15)

Alkyne end-functionality was confirmed by the observation of a signal at 4.68 (CH≡CC*H*$_2$OC=O) in the ^{1}H NMR spectrum (Figure 4.7). $M_{n,NMR}$ (2460 g/mol) of

the polymer was determined accordingly from the integration of the peaks at 4.07 and 3.66 ppm related to PCL repeating unit and CH_2OH, end group protons of PCL, respectively.

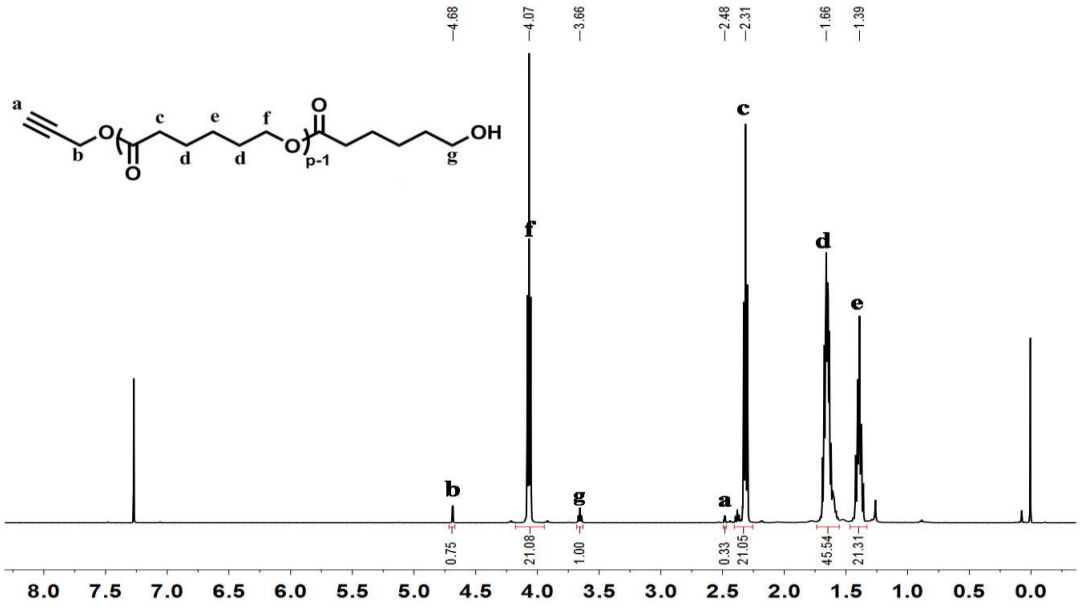


Figure 4.7 : ^{1}H NMR spectrum of Alkyne-PCL in $CDCl_3$

CuAAC reaction was carried out between PC-azide$_7$-*co*-anth$_{10}$, and **14** in the presence of Cu(I)/PMDETA in DMF at room temperature for 24 h to yield the final product, PC-*g*-PCL.

PC-azide$_7$-*co*-anth$_{10}$ copolymer formation was obtained by FT-IR spectroscopy. The weak streching due to azide at 2094 cm^{-1} disappeared and the sharp streching due to carbonyl of PCL at 1745 cm^{-1} appeared after graft formation (Figure 4.8).

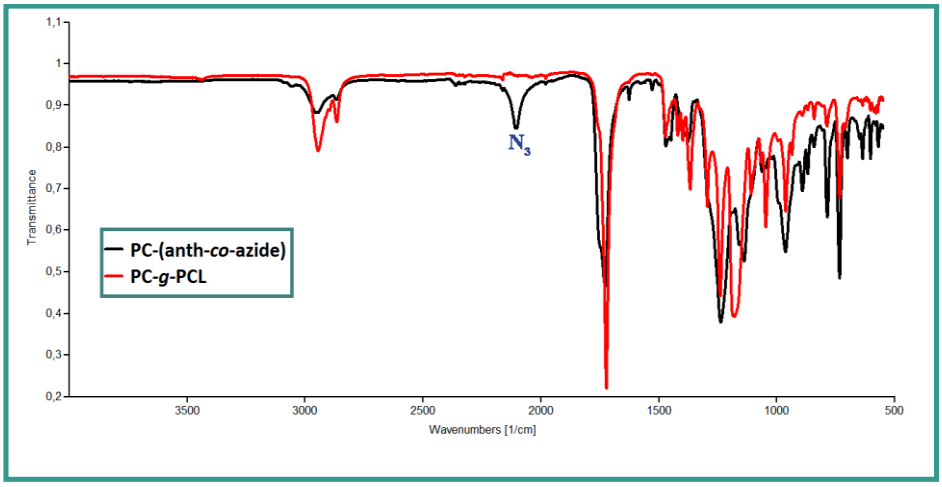


Figure 4.8 : FT-IR spectra of PC-azide$_7$-*co*-anth$_{10}$ (red) and PC-*g*-PCL (black)

NMR analysis showed that precursors **14** had successfully been grafted to the copolymer (Figure 4.9). The peaks at 8.51-7.45 ppm could easily be assigned as Ar*H* of anthracene and C*H* of triazole. Additionally, a new peak appeared at 4.07 ppm and expansion of peaks at 3.65 ppm and 1.39-1.66 protons of PCL.

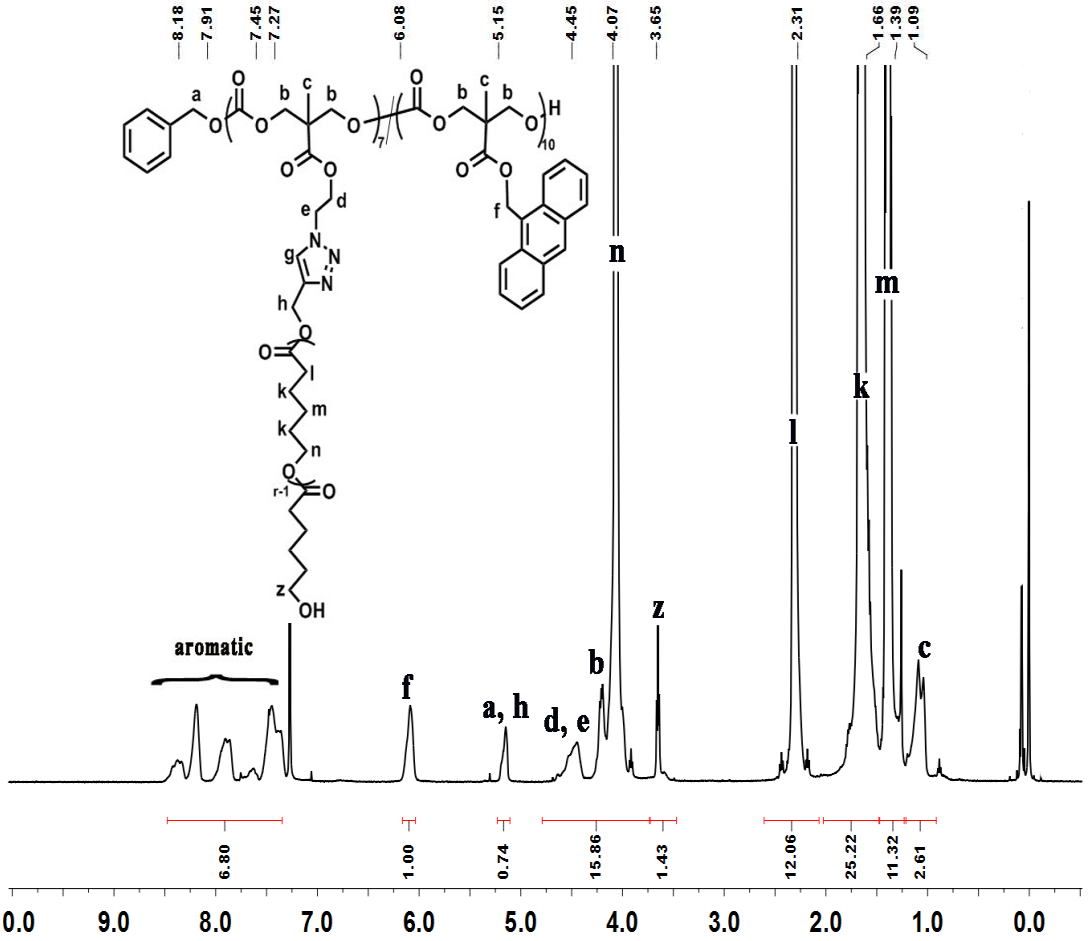


Figure 4.9 : ^{1}H NMR spectrum of PC-*g*-PCL copolymer (from PC-azide-*co*-anth and Alkyne-PCL) in $CDCl_3$ (500 MHz).

$M_{n,GPC}$ of PCL-alkyne was calculated to be 7340 g/mol, based on linear PS standards (RI detector). However, determining more precise the molecular weight for PCL, a correction formula was used: $M_{n,PCL} = 0.259 \times M_{n,GPC}^{1.073}$ ($M_{n,PCL}$ = 3640 g/mol), where $M_{n,GPC}$ is the molecular weight determined from GPC using PS standards. $M_{n,NMR}$, and $M_{n,PCL}$ values were in good agreement.

4.4.2 Diels-Alder click reaction between PC-*g*-PCL and PEG_{550}-MI

First, PEG_{550}-MI was obtained via an esterification reaction between Me-PEG (*M*n=550) and excess amount of **3** in the presence of DCC as a coupling agent and DMAP as a catalyst (4.10).

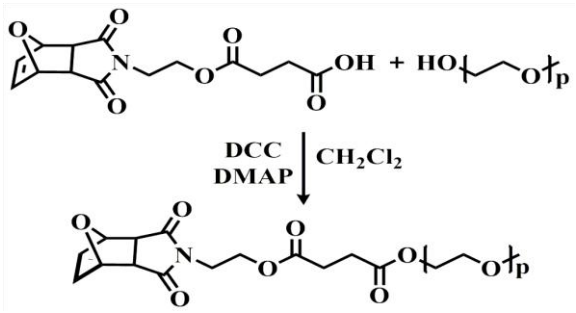


Figure 4.10 : ^{1}H NMR spectrum of PEG-MI in $CDCl_3$ (500 MHz).

From ^{1}H NMR spectrum of the polymer, the bridge and bridge-head protons were detected at 6.50, 5.24 and 2.86 ppm respectively. The $M_{n,NMR}$= 750 of MI-PEG was determined from a ratio of integrated peaks at 3.62 ppm (OC*H*2C*H*2 protons of PEG) to 6.50 ppm (vinyl end protons).

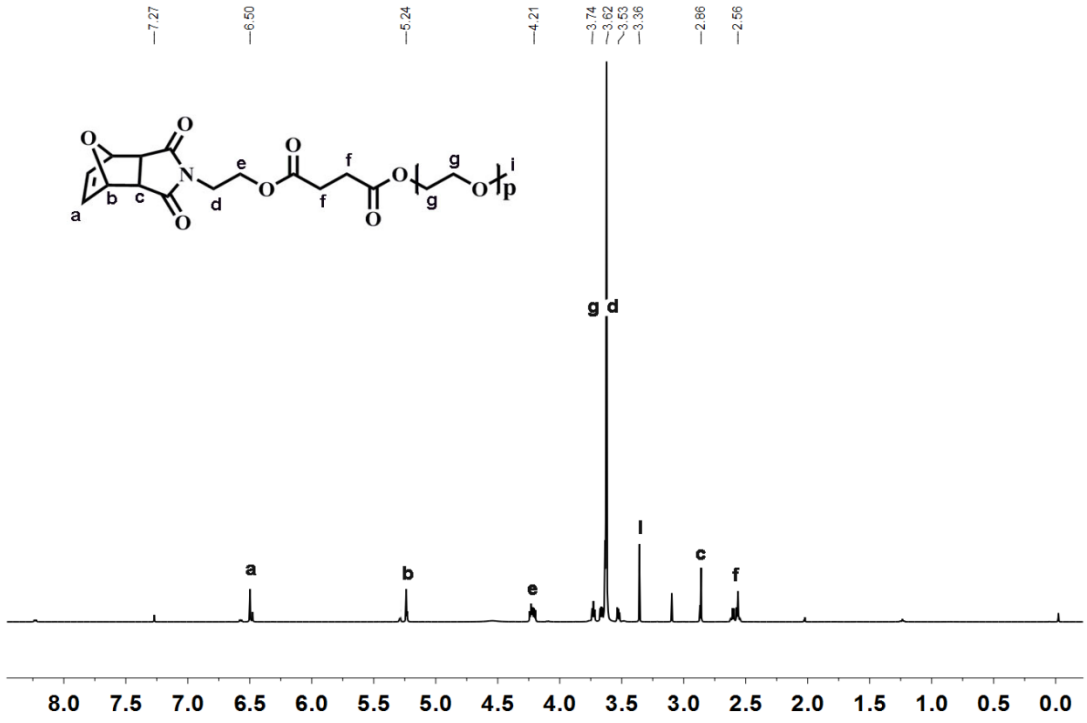


Figure 4.11 : ^{1}H NMR spectrum of PEG_{550}-MI in $CDCl_3$(500 MHz).

The PC-*g*-PCL polymer was subsequently ligated with well-defined α-furan-protected maleimide-terminated linear polymers, PEG_{550}-MI, in order to yield well defined PC graft copolymers under Diels-Alder reaction conditions. The 13 equiv of the α-furan protected maleimide-terminated homopolymers with respect to the PC-*g*-PCL were deliberately chosen to ensure the reaction completion, as well as easy elimination from the reaction mixture. The Diels-Alder adduct was monitored by UV spectroscopy by following the disappearance of the characteristic five-finger

absorbance of the anthracene moiety at 300-400 nm and thereby, Diels-Alder efficiency (DAeff) was calculated to be 93% by UV measurements with a ratio of final absorbance (A_t)at 48 h and initial absorbance (A_0); DA *eff*= **(**1-A_t/A_0)x100 ($M_{n,NMR}$= 27310, $M_{n,GPC}$= 28237).

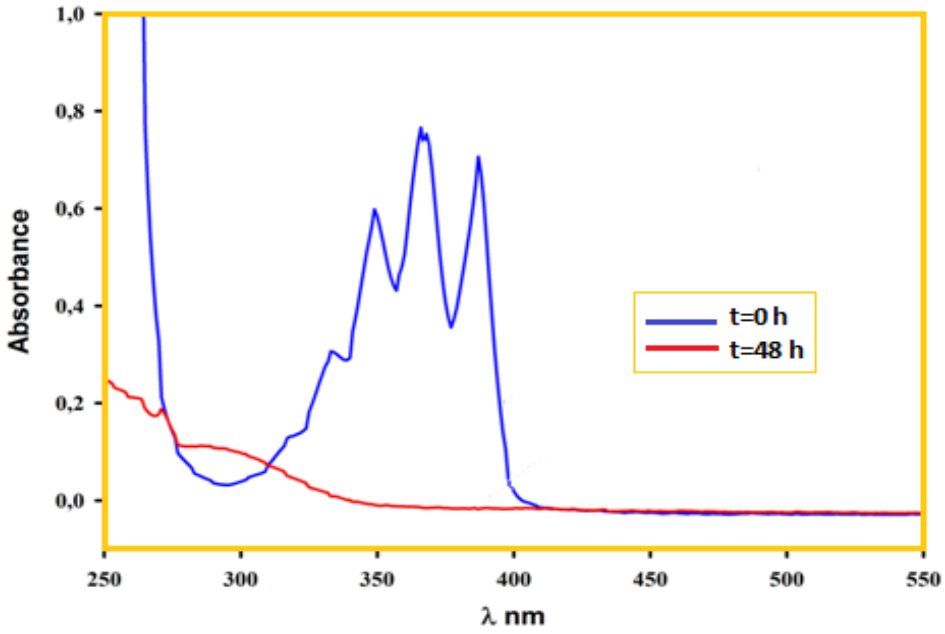


Figure 4.12 : UV-Vis spectra of PC-*g*-PCL-PEG

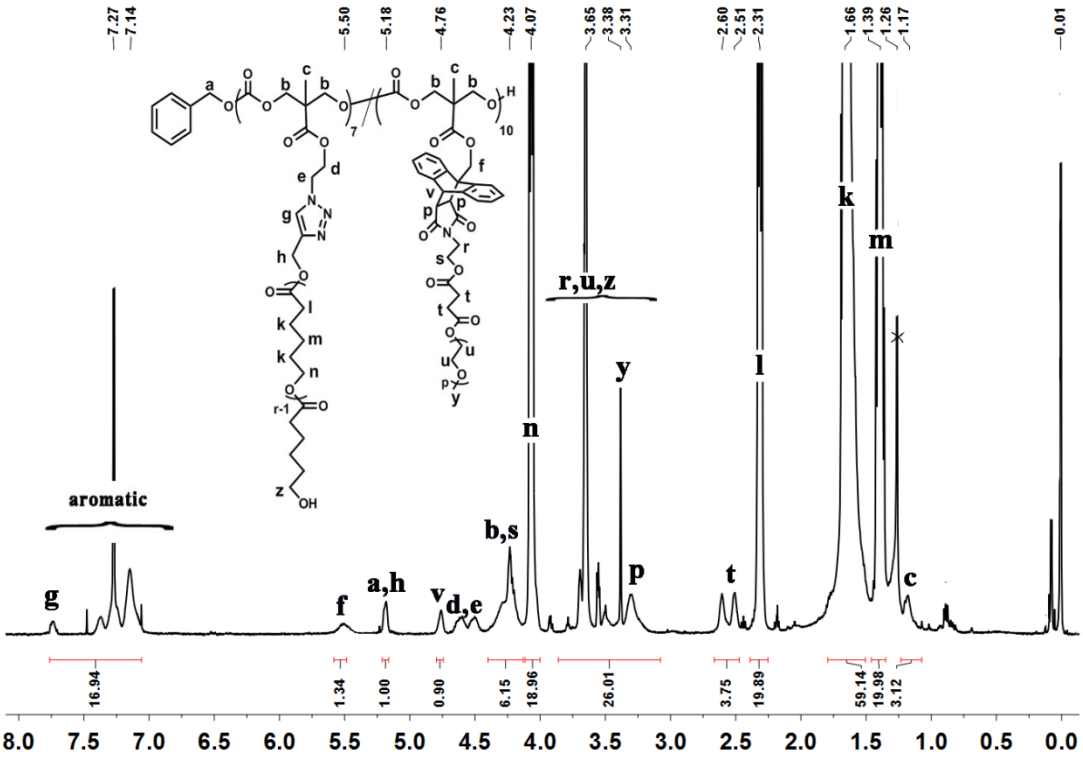


Figure 4.13 : ^{1}H NMR spectrum of PC-*g*-PCL-PEG copolymer (from PC-*g*-PCL and MI-PEG) in $CDCl_3$ (500 MHz).

The appearance of new signals corresponding to the OCH_2CH_2 at 3.65 ppm, NCH_2CH_2 at 3.38 and 0CH_3 at 3.31 ppm confirmed the structure of the functionalized copolymer (4.13).

After purification the PC based heterograft copolymers, a shift to the higher molecular weight region was detected from GPC measurements while maintaining narrow polydispersity index (M_w/M_n) (4.14).

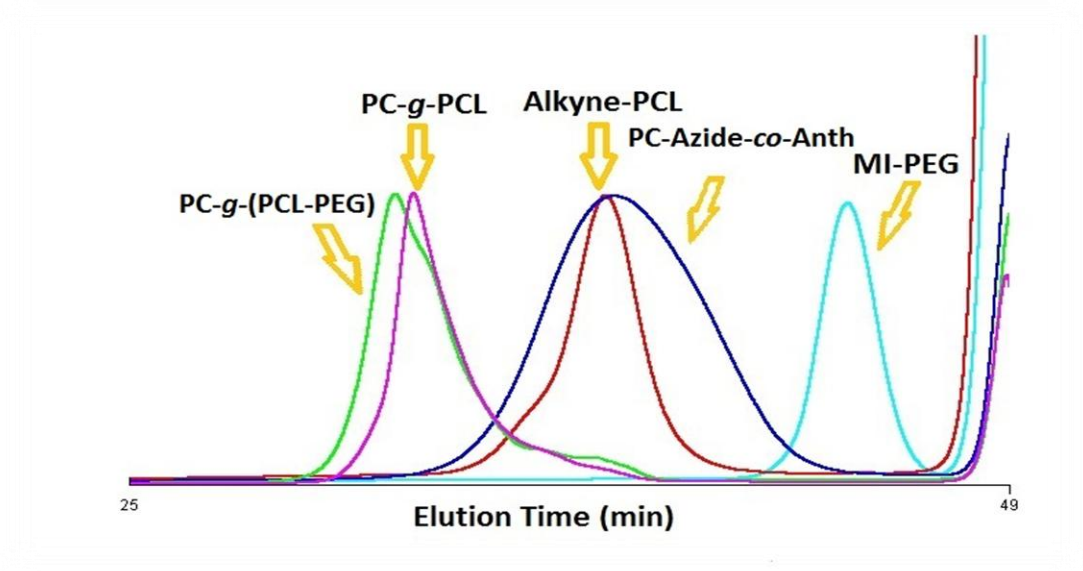


Figure 4.14 : Overlay of GPC traces of MI-PEG, Alkyne-PCL, PC-azide-*co*-anth, PC-*g*-PCL and PC-*g*-PCL-PEG in THF at 30°C.

Table 4.1: Characteristics of PC-graft copolymers via sequential synthesis

Polymer	$M_{n,GPC}$[f] (g/mol)	M_w/M_n[f]	$M_{n,NMR}$ (g/mol)
MI-PEG[a]	840	1.09	750
Alkyne-PCL[b]	3640	1.08	2460
PC-azide$_7$-*co*-anth$_{10}$[c]	6550	1.39	5110
PC-g-PCL[d]	32370	1.40	24710
PC-*g*-PCL/PEG[e]	37180	1.68	29760

[a]Obtained by an esterification reaction between compound PEG-OH (550) and **(13).**
[b] Synthesized by ROP of ε-CL in CH_2Cl_2 using DBU as a catalyst and **(14)** as an initiator at 110 °C. $[M]_0:[I]_0 = 30$
[c]Synthesized by ROP of **(15)** in CH_2Cl_2 using DBU and TU as a catalyst and benzyl alchol at 30 °C.
[d]From alkyne-PCL
[e]From MI-PEG
[f] Determined by GPC (RI detection) in THF at 30 ºC using PS calibration

5. CONCLUSION

In this study, we described the synthesis of well-defined PC-based graft copolymers using the copper catalyzed azide-alkyne cycloaddition (CuAAC) reaction of the PC-azide-*co*-anth with alkyne-PCL. Then we prepared Diels-Alder click reaction with α-furan protected maleimide-terminated polymer (PEG_{550}-MI). UV spectroscopy indicated that DA efficiencies of the reactions were quantitative. Moreover, both GPC and ^{1}H NMR analysis confirmed a successful graft copolymer formation. Therefore, the Diels-Alder click reaction is found to be superior over the classical preparation of PC-graft copolymers via growing graft from the hydroxyl-terminated macroinitiator using only ROP. Notably, Diels-Alder reaction becomes a more prominent particularly for the preparation of a variety of biocompatible polymers (such as PC.). Diels-Alder, and CuAAC reactions have offered the synthesis of well-defined more complex macromolecular architectures in sequential way.

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